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A. M. BUTLEROV

(1828–1886)

THE 125TH ANNIVERSARY OF THE BIRTH OF THE FOUNDER OF THE THEORY OF CHEMICAL STRUCTURE AND OF THE SYSTEMATIC SYNTHESIS OF ORGANIC COMPOUNDS

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The scientific acitivity of Aleksandr Mikhailovich Butlerov covering the period between the fifties and the eighties of the last century, was already highly acclaimed by his leading contemporaries. The further we move from the years of his activity the clearer it becomes that his scientific studies directed organic chemistry to new routes of multistage synthesis, to the investigation of isomeric, tautomeric and polymeric transformations, to the establishment of the chemical structure of complex compounds, and to the clarification of the mechanism of chemical reactions.

The theoretical and experimental investigations of A. M. Butlerov are characterized by innovations and great penetration. They astonish us by the wealth of their scientific insight, originality and experimental accuracy, by their most valuable discoveries and undertakings. The most important experimental results of his researches were directed toward the founding and development of the theory of chemical structure which for upward of 90 years has had a profound and progressive influence upon the development of organic chemistry and the whole of chemical science. The theory of chemical structure, whose author was A. M. Butlerov, must be regarded as one of the greatest generalizations of science.

In the past the great services of A. M. Butlerov in the theoretical field have sometimes been underrated and even forgotten. Even today the same lack of appreciation of his work may be noticed. It must therefore be emphasized that Butlerov is indeed the founder, the architect of a theory of chemical structure differing fundamentally and in principle from the previous theoretical concepts [1].

Science is indebted to him for the logical application of the principles of materialistic philosophy to the study of the structure and properties of molecules.

Characteristic of Butlerov is the materialistic and even dialectical solution of the fundamental problems of organic chemistry in contrast to the unrealistic eclectic and idealistic approaches of Gerrard, Kekulé, Kolbe, Berthelot and other great chemists of the mid-nineteenth century to the fundamental chemical problems.

The 125th anniversary of the birth of Butlerov fell on September 6, 1953 (he was born on August 15, 1828 in the town of Chistopol, Kazan province): it is memorable not only because of the work of the great scientist but also because the intervening 125 years have been a notable historical period in the development of organic chemistry. This is true in particular of the last 90 years, after Butlerov's theory of chemical structure had been confirmed by him in collaboration with his students in the sixties.

The growth of industry and the development of capitalism (also in Russia) from the second quarter of the nineteenth century led to more and more new problems in the chemistry of organic compounds. A very active study of natural organic compounds commenced and there was rapid development of the branches of industry involving the chemical processing of natural products such as bituminous coal (illuminating gas), petroleum, starch (K. S. Kirchoff, 1806-1815) and others. But after Butlerov's theory of chemical structure had become generally accepted as

a basic principle of organic chemistry, the vast material of that science was brought into a harmonious system and the systematic laboratory and industrial synthesis of organic compounds was developed.

Toward the end of the twenties of the nineteenth century, when Butlerov was born, organic chemistry had already collected not a few valuable observations and discoveries; the composition and properties of important natural compounds such as fats were being industriously studied.

The first three decades of the past century and the subsequent years up to the start of the sixties constituted a preparatory period in the development of the theoretical ideas of organic chemistry which rounded off the Butlerov theory of chemical structure.

The forties to the sixties was a period in which interest was shown not only in the systematics and classification of the very many organic compounds that were already known, but also in the problems of linking and arrangement of atoms in the molecules of organic substances. Between the sixties and the death of Butlerov (1886) organic chemistry was enriched by notable theoretical and experimental researches of Butlerov himself and his pupils. Even during his lifetime the enormous significance of the theory of chemical structure had become manifest and the discoveries which had been made by Butlerov himself in the experimental field were beginning to be widely disseminated.

Butlerov's theory of chemical structure was further developed in the field of stereochemistry by the investigations of Louis Pasteur, Van't Hoff and Le Bel, Wislicenus and others, while Butlerov himself made a valuable contribution to the concepts of the spatial distribution of atoms in molecules.

Taking into consideration the great revolution in chemistry and the vast perspectives revealed to synthetic organic chemistry through Butlerov's theory of chemical structure, we can distinguish the following fundamental stages in the history of organic chemistry:

1) The pre-Butlerov period (before the start of the sixties of last century)—a period of accumulation of the most important experimental facts and of the creation of a classification of organic compounds (homologous series, etc.); in this period various conflicting ideas were reconciled by several fundamental concepts of chemistry and some basic ideas were developed for the future theory of organic chemistry.

2) The Butlerov period—the period of creation and introduction into science of the theory of chemical structure and the development of stereochemistry on its basis.

3) The post-Butlerov period, marked by the extensive development of the organic synthesis of new compounds and of the important substances of the vegetable and animal kingdoms, as well as by the strengthening of the theory of chemical structure with special reference to the reciprocal effects of atomics and groups of atoms in molecules.

A. M. Butlerov began his work as an experimental and theoretical organic chemist in the fifties, in a period of sharp controversy in scientific chemical ideas, and he fertilized the researches of his contemporaries by indicating new vistas and the great potentialities of chemical development.

As a scientist, Butlerov grew up at Kazan University [2] as a student of eminent chemists: K. K. Klaus, discoverer of the element ruthenium, and N. N. Zinin, famed for the reduction of nitrobenzene to aniline and other reactions.

Starting to deliver lectures at Kazan University at the age of 21-22, Butlerov at once distinguished himself as a talented and versatile lecturer. At the early age of 26 he was chosen as professor at Kazan University where he worked from 1850 to 1869. In 1869, when we was called to Petersburg University as professor, began the not less glorious Petersburg period of his activity as a scientist and teacher. In Petersburg, just as in Kazan, Butlerov directed research in the laboratory and was always surrounded by numerous students. In 1871 he became a member of the Russian Academy of Sciences, and in 1874 he was elected academician extraordinary.

With his penetrating philosophical intellect and great mastery of experimental chemistry, Butlerov founded the renowned Butlerov school of science whose representatives were found first in Kazan and later in Petersburg University and the Academy of Sciences.

The members of the Butlerov school were the pride of our science.

Brilliant lecturer, talented teacher and inspired scientist, he rendered great service to the teaching and development of organic chemistry in Russia.

A. M. Butlerov combined scientific work with serious social activity, thus following the custom of the progressive Russian Intelligentsia – "six decades" in the national interest.

He undertook much public work as professor and rector of Kazan University, as professor at Petersburg University and as Academician (in the latter capacity as active member), and as President between 1879 and 1882 of the Russian Physicochemical Society, as Chairman of the Free Economic Society and propagandist of efficient bee-keeping, as a great worker for the education of women, and so on.

Aleksandr Mikhailovich Butlerov – scientist-patriot, scientist-citizen – fought both in the university and in the Academy for the interests of Russian science with great rectitude and passion.

A. M. Butlerov died suddenly at the age of 58 on August 17 (Old Style August 5), 1886 in the village of Butlerovko in the Spassky district of Kazan province where he was also buried.

Chemists of the Soviet Union are assiduously engaged in the development of the theory of chemical structure, working fruitfully in the field of organic synthesis for the solution of the most important theoretical and practical problems.

In connection with the 125th anniversary of the birth of our great compatriot, A. M. Butlerov, Soviet chemists with great gratitude again take note of the most important of his scientific researches from which stem the great achievements of organic chemistry in the USSR.

1. The Molecular-Atomic Constitution of Substances and the Atomic Weights of the Elements According to Butlerov's Ideas

In his scientific work Butlerov was a materialist who regarded a compound as being in movement and in growth. In his researches it is not difficult to see the logical application of atomic-molecular concepts. Only with firm belief in the reality of molecules and atoms was it possible for Butlerov to expound the concept of the strictly determined chemical structure of chemical compounds and of the representation of the composition and structure of a molecule by a unique chemical formula.

In his communication of 1885 [3] we find the following opinions: "The atom is just as real an entity as the molecule" and "In our opinion we must speak of atoms as if they were real objects".

Being convinced that the chemical elements are formed from simpler component particles, Butlerov arrived at the conclusion that certain variations in the atomic weights of elements were possible, as also (in consequence) deviations of the composition of chemical compounds from the law of constant proportions. In the laboratory Butlerov (1882) carried out experiments aiming at clarification of this – for his day – complex problem; these were broken off by his unexpected death.

Butlerov thus made a new approach to the problem of the concept of the chemical element. This fundamental concept had undergone profound changes [5] in the course of centuries; it acquired new features with the discovery of radioactivity and the detection of isotopic phenomena which had been so astonishingly predicted by Butlerov.

Very effective tools for the establishment of differences in the mass of atoms were the physical methods of investigation developed in recent times and stemming directly from the Crookes tube which A. M. was the first to demonstrate in Russia in 1880 at a conference of the physics division of the Russian Physico-Chemical Society. In his ideas on isotopy Butlerov was 30 years in advance of the science of his day.

2. Chemism is Movement

The works of Butlerov ("Introduction to the complete study of organic chemistry" [6], etc.) contain his views on chemical affinity and the units of valences of the elements. These are interesting as a reflection of the ideas of this time on these important questions which even today have not been conclusively solved. Very important, however, is his general dictum in regard to chemical phenomena: "Chemism is movement".

According to Butlerov, therefore, chemical phenomena are a special form of motion which may be manifested in thermal, optical and electrical phenomena. He draws attention to the "importance of the relation between the chemical action of electricity and the concept of atomicity which plays such an important part in chemical theory" and to the equivalence between electricity, heat, chemism and visible mechanical work. In opposition to Berzelius he did not consider it possible to equate chemical phenomena with electrical phenomena but held the opinion that chemism is a more general and complex form of motion. It must be remembered that,

according to Butlerov, the atoms entering into the composition of molecules are in continuous movement [7]. "We look upon a chemical compound not as on a dead and motionless thing; we assume, on the contrary, that it is endowed with constant movement; this is true also of its minutest particles whose reciprocal relative continuous movements are resolved into a certain constant average result." However, as long as a given substance exists, this movement of the atoms is executed with maintenance of the previous "order of the chemical bond between the atoms in the molecule, and this constitutes the chemical structure of the substance".

"We provisionally say" —we read in another of his communications (1885) [3]—"that atoms are combined or joined with one another, but we definitely do not thereby imply that the atoms actually grip one another or that they are relatively immobilized."

In his communication (in Speyer in 1861) [8] on the theory of chemical structure, Butlerov reasoned about the linkage strain in polyatomic molecules on the assumption that it may change "according to the nature of the actual substances and according to the conditions in which the action takes effect." Consequently, a difference in the units of affinity of carbon could be assumed. At first, as long as it was not known that ethyl hydride and dimethyl were both ethane (this was established in 1864 following the work of Schorlemmer), and as long as other cases of suggested isomerism had not been clarified, Butlerov suggested the hypothesis of different units of affinity in polyvalent elements. But after starting a more detailed study of the isomerism of hydrocarbons, he arrived at the conclusion that the isomeric parafinic hydrocarbons can only differ in the structure of the hydrocarbon sketeton. In the paper on "the affinity of polyatomic partners" [9] we see the transition from his concept of the difference in units of affinity to the idea of the mutual influence of atoms constituting a molecule: "Here and now, when speaking of the difference in units of affinity, it is impossible not to point to the influence which is exreted on the properties of one set of units of affinity by the nature of the partners linking the other units, and it is even necessary to add that the difference is perhaps governed by this influence."

Butlerov afterwards expressed himself several times in opposition to the hypothesis of difference of units of affinity when deriving possible structural isomers; thus he criticized the application of this hypothesis by Kekule who had erroneously written of the existence of three propyl alcohols (1865-1866). This hypothesis was for a long time adhered to by Erlenmeyer who was a follower of Butlerov in questions of the theory of chemical structure. On the same basis Kolbe erroneously reported the existence of two methylpropyl ketones. When triphenylmethyl, tribiphenylmethyl, etc., became known, their existence was ascribed to the phenyl and (in particular) the biphenyl radicals attracting more affinity to themselves than usual from the carbon atom of methane. Reference began to be made to the differing affinity capacity (capacité affinitaire) of radicals, i.e., the differing consumption of the affinity of the carbon atom by different radicals (A. Werner) [10].

In his last communication to the Academy of Sciences (1943) A. E. Favorsky [12] returned to the hypothesis of the different quotas of affinity disbursed by the carbon atom in binding different substituents, but he modified the hypothesis by introducing the concept of a supplementary affinity of the carbon atom.

Much attention was given in the twenties and thirties of the present century to the question of the affinity capacity of different radicals.

Many authors have arranged radicals in order of affinity capacity on the basis of many reactions and not infrequently with conflicting results. Thus in the dehydration of glycols and the isomerization of aldehydes to ketones we obtain contradictory series in respect of migration ability and affinity capacity [11].

The concept of the affinity capacity of atoms and radicals, as formulated by A. Werner, as well as the idea of the changing "strain" of chemical bonds or the difference in relative magnitude of the consumed affinity about which both Butlerov and Erlenmeyer speculated (to some extent also Kolbe —in respect of carbonic acid) may be expediently considered in the light of the electronic hypothesis of the variation in the density of the electron cloud which varies for different atoms, i.e., the so-called electron density.

Butlerov established [13] that, contrary to Erlenmeyer's view, isomerism in the light of the theory of chemical structure is not the result of a hypothetical difference in the units of affinity attached to polygenic atoms.

Butlerov's idea of the mobility of atoms in a molecule ("dynamics, not statics") was clearly expressed in his theories of isomeric and tautomeric phenomena which A. E. Favorsky later described in the concept of equilibrium isomerism [14] and illustrated by his own experiments (transformations of mono- and dibromohydrins of alcohols, reversible isomerization of mono- and disubstituted acetylenes and allenes). He showed that isomeric transformations also acquire an equilibrium character in certain conditions, as is typical of tautomeric phenomena.

Butlerov persistently directed attention to the importance of applying dynamic ideas to chemical phenomena. Butlerov gave the following definition of a chemical compound [7]: "A chemical compound constitutes a specific relation between the movements of the atoms in a molecule."

The actual existence of the very same number of isomers for a given structure as is predicted by the theory of chemical structure is a most vivid confirmation of the theory of chemical structure.

Butlerov and his pupils started a close study of the isomeric transformations accompanied by rearrangement of atoms in a molecule. The first (and clear) example of intramolecular rearrangement of a carbon skeleton (1874) was the pinacolin rearrangement [15]. Even earlier (1868) Butlerov had noted the formation of a secondary alcohol instead of a tertiary one, in the organozinc synthesis [16]. The study of isomeric transformations was very extensively developed by A. E. Favorsky and his school.

Discussing the formulas [17] of cyanic acid and urea, Butlerov in 1862 arrived at the conclusion that for cyanic acid we may picture "the still existent but transient phase of its structure which may exist, for example, during conversion of cyanic acid into carbon dioxide and ammonia".

In studies [18] on "isodibutylene" (diisobutene) interesting conclusions were reached in connection with the problem of the addition of water to olefinic hydrocarbons and the reverse process which is accompanied by isomerization: "We think that even in the absence of a catalyst (which may be sulfuric acid in this example) the molecules of some substances, due to the constant breakdown and re-formation of products in a fresh order, are constantly isomerizing, changing from one modification into another—and conversely." Butlerov's great scientific perspicacity suggested to him the possibility of an equilibrium shift in a specific direction, a process found to be characteristic of the equilibrium mixture of tautomeric substances: "The mass of a compound contains particles with different structures (say two) and when these molecules are susceptible to rearrangement the whole of this mass will naturally undergo reactions characteristic of one of the structures or reactions characteristic of the second structure, depending upon the nature of the reagents employed, i.e., depending upon the direction of the effect of this reaction."

In 1885 Laar [19] proposed the term "tautomerism" for the phenomena discovered by Butlerov, but Laar idealistically misinterpreted them by attributing an oscillating character to the transformations and a multiple molecular structure to the molecules of one and the same substance, instead of speaking about an equilibrium mixture of tautomeric compounds.

3. The Chemical Structure of Molecules and Its Representation by Chemical Formulas

A fundamental law of chemistry was formulated in Butlerov's theory of chemical structure: Inherent in each chemical compound is a strictly defined order of the reciprocal chemical linking of the atoms constituting its molecule, all the properties of a compound being governed by its chemical structure, while the chemical properties of the atoms and groups of atoms in the molecule—linked to one another or not directly linked—depend on their reciprocal effects and the external conditions.

Chemical structure is established unambiguously by chemical (synthetic and analytical) and physical methods. A chemical formula—one unique for each chemical compound—must reflect "the mode of the mutual chemical bonding of the elementary components (atoms) in the molecule". Butlerov also wrote [6]: "It would be correct, in the present state of knowledge, to apply the term 'rational formulas' only to formulas which reflect the chemical structure of molecules."

The problem of the arrangement of atoms in a molecule, already posed in a general form by M. V. Lomonosov, began to receive ever increasing attention after the development of methods of quantitative analysis of organic compounds and the introduction of chemical formulas for the elementary composition with representation of each chemical element and its relative amount by the first letters of the Latin name (Berzelius, 1813).

On the basis of the old radical theory, which merged with the electrochemical hypothesis of Berzelius, chemical formulas indicated two simple or more complex portions which, so to speak, "preexist" in the molecule in question. Thus, the formula of saltpeter would indicate that potassium nitrate consists of anhydrous nitric acid and potassium oxide, while the formulas of organic compounds are represented by "preexistent" radicals for which an independent existence was originally postulated.

In our own time the application of the idea of "preexistence" of one complex body in another can be seen in the usual formulas of molecular compounds. Characteristic of typical complex compounds are more complex relations between the components of the molecule, but also in these formulas a sort of "preexistence" is attributed to

simpler molecules in the compounds (in ammines, hydrates, etc.).

The problem of molecular compounds has been adequately clarified by A. Werner's theory with reference to typical complex compounds.

Concerning compounds for which it is difficult to decide "whether we are dealing with chemical molecules or aggregates of molecules which adjoin one another", Butlerov [7] spoke as follows (1879) about molecular compounds: "We have no criteria as yet for strict demarcation of a chemical molecule from an aggregate of molecules, while the transition of the latter into solutions, etc., is quite gradual and imperceptible."

We know that physicochemical analysis in the hands of D. I. Mendeleev, N. S. Kurnakov and their pupils made a valuable contribution to our understanding of solutions, melts, and molecular compounds.

According to Gerard's unitary theory, in harmony with Liebig's theory of polybasic acids, the suggestion was made of the "preexistence" in sulfuric acid of sulfur trioxide and water, while salts were regarded as constituted by metallic oxide and acid; the molecule was thus regarded as a unit. The unitarists had a different conception of organic compounds. "Radicals (wrote Butlerov apropos of the unitary theory) are those groups which are encountered in the composition of different complex substances; they have the ability to be transferred by certain reagents from one substance to another and may thus be regarded as replacing certain elementary particles" [6].

The formulas consequently indicated that in a typical substance (hydrogen, water, hydrogen chloride, ammonia) the hydrogen atoms are replaced by organic radicals. However, the concept of types, according to Butlerov, "does not represent an inherent, material subscription to the unitary theory but a close merging with the latter" [6].

The principle of substitution found wide application in organic and inorganic chemistry, especially with the introduction into science of the doctrine of atomicity of elements (Frankland, 1852; Odling, 1854, etc.). In particular, the quadrivalence of carbon was established by Kekulé and Kolbe. Dumas equated the substitution principle with Mitscherlich's doctrine of isomorphism, but the similarity is remote.

Kolbe, who for a long time remained an adherent of the theory of radicals and an opponent of the theory of chemical structure, combined the former with the ideas [?] of substitution which he used extensively and in some cases with successful results. He pointed to the possibility of existence of secondary and tertiary alcohols (1859), and effected substitution of the hydrogens in a radical of a simpler alcohol by other radicals. But by utilizing arbitrary methods in applying the substitution principle, he frequently fell into error, as for instance in assuming the existence of two methylpropyl ketones.

In Butlerov's paper (1864) [20] "on the systematic application of the principle of atomicity" to the prediction of isomerism and metamerism, we find the following passage: "How faulty become derivations when substitution is brought into the foreground and the theory of chemical structure (constitution or points of application of affinity) is put on one side."

N. A. Menshutkin [21] for a long time expressed himself (1878, 1885) against the theory of chemical structure and attempted to show that the isomerism of hydrocarbons can be quite satisfactorily explained by the substitution theory without reference to the theory of structure.

The French chemist Berthelot, who had acquired a great reputation in the first half of the 19th century by his successful syntheses of simple organic compounds, adhered in the sixties to the eighties [3] to the same theory of substitution in a slightly modified form (known as the theory of generators); according to his theory, the constitution of a compound is represented by the equation of its formation from a selected generator. Berthelot explained the different properties of isomers by differences in generators (starting substances) and not by different chemical structures.

Berthelot's criticism of the theory of chemical structure was described by Butlerov (in his 1879 paper) as "not chemical realism"; his evaluation of Berthelot's views was summed up in the phrase "chemical nihilism".

The principle of substitution is fundamentally correct, and in the case of simpler compounds, it provides graphic examples for teachers, as is evident for instance from D. I. Mendeleev's utilization of the principle of substitution in "Principles of Chemistry" in the derivation of nitrogen derivatives. However, the principle of substitution, as Butlerov correctly pointed out, is a narrower concept, of secondary importance in comparison with the theory of chemical structure.

In recent years Yu. A. Zhdanov [22] and others have drawn attention to the previously ignored materialistic-dialectical aspect of the theory of chemical structure and to Butlerov's concept of the chemical formula as the

reflection of the actual order of the chemical linking of atoms in a molecule. Apart from the immediate pupils [23] of Butlerov such as V. V. Markovnikov, many authors [24] have paid high tribute to the tremendous achievement of Butlerov in firmly introducing into science the theory of chemical structure, but they have not properly demarcated the theory of chemical structure from the doctrine of the valence of elements, from the ideas of the linking of atoms in the molecule, from the principle of substitution and from other inferences from previous theoretical views (homologous series, the concept of radicals) utilized by Butlerov in his theory of chemical structure.

A. M. Butlerov enunciated original ideas on the following aspects:

1) The specific order of chemical bonding of atoms in a molecule.

2) Methods of establishing chemical structure by synthetic, analytical and physical methods.

3) Strict demarcation of the problem of chemical structure in the sense of the order of chemical bonding of atoms from the problem of the spatial arrangement of atoms (constitutional concept of Laurent). Butlerov proposed the tetrahedral model of the carbon atom before Van't Hoff and Le Bel. Butlerov thereby clearly expressed the necessity of explanation of the existence of "physical isomers" (optically active and other isomers) from the standpoint of the spatial arrangement of atoms in the molecule; this must be regarded as a development of the theory of chemical structure.

4) Isomerism as an inevitable consequence of the definite chemical structure of compounds of saturated and unsaturated types with a clear formulation of the concepts of double and triple bonds.

5) Tautomeric, isomeric and polymeric transformations (associated with states of equilibrium) as a consequence of the dynamism of atoms in the molecule which leads to the compounds which are most stable under the given conditions.

6) The doctrine of the chemical formula as the representation of the actual order of the chemical bonding of atoms in the molecule.

It is true that the theory of substitution and the theory of types, and indeed the unitary system and the old theory of radicals and substitution (Kolbe), in no way conflicted with the principle that each chemical compound must be characterized by a single formula. Nevertheless, Gerrard, Kekule and the other "typists" made an unrealistic and generally idealistic approach to this problem. Gerrard stated that we only know the past and future molecules resulting from chemical reactions and not the present molecules. Gerrard and later Kekule (after 1861) considered that as many formulas may be attributed to a chemical compound as there are methods for its preparation. In his 1861 report [8], however, Butlerov wrote: "If we now attempt to specify the chemical structure of substances and if we succeed in expressing it by our formulas, then these formulas will be (not completely but to a certain degree) real and rational formulas. In this sense only one rational formula will be possible for each compound."

In the pages of our chemical [25] and general-philosophical journals, as well as in many symposia [26] it was shown that the polystructurality of the resonance and mesomeric formulas, like the "resonance" of Wheland and the "mesomerism" of Ingold, are completely fallacious and idealistic concepts devoid of any basis in quantum chemistry and radically in conflict with Butlerov's theory of chemical structure.

The representation of the structure of any chemical compound by two formulas between which, as it were, the true structure lies is entirely pointless because each compound is different from any other and the formula expresses the chemical structure. Consequently, the conclusion (in the sense of V. A. Izmailsky's mesomerism) that the structure of a given substance lies between two certain structures, i.e., between two formulas, is meaningless [26]. As long as a chemical structure is not fully proved, we may propose hypothetically one or several formulas.

Chemical structural formulas express the order of the chemical linking of atoms on the basis of a study of the chemical and physical properties of compounds, and therein resides their value for chemistry. There is no doubt also that spatial formulas in organic chemistry and in the chemistry of complexes adequately represent the true geometrical relations of the atoms in molecules.

For the representation of the chemical structure of experimentally prepared molecules, Butlerov made use of the valence concept (Odling, Frankland), of the principles of substitution and of the concept of linking of atoms formulated in the papers of Kekule (1858), Couper (1858) and Loschmidt (1861). Only Couper (before 1861), however, and not Kekule applied the theory of linked atoms to the representation of formulas, and even these formulas bore a formal and abritrary character. Butlerov gave proved chemical formulas for a series of compounds and — on the basis of this materialistic theory of chemical structure —he demonstrated the predictive value of the formulas of the theory of chemical structure in regard to isomers as early as 1863. Finally, the derivation of chemical

formulas is founded on the doctrine of the atomic-molecular constitution of substances, of atomic weights and of valence. Butlerov said in his communication of 1885: "What would be the significance, we may ask, of any one of our formulas with its atomic symbols if the concept of the atom did not represent some specific reality for us?"

While representing the order of the chemical bond of atoms, the usual structural formulas do not picture those reciprocal effects of atoms and atomic groupings which are dependent on the chemical structure and the nature of the atoms and which are characteristic of molecules in given conditions. Since the time of Butlerov and Markovnikov, whose work led to the adoption in organic chemistry of the doctrine of the reciprocal influence of atoms, very many diverse rules have accumulated in regard to the mutual influence of atoms, reactive groups and radicals. In this connection Butlerov said: "When general laws become known for the dependence of the chemical properties of substances on their chemical structure, then such formulas (i.e., real rational formulas in Butlerov's sense) will be the expression of all these properties".

In connection with electronic concepts in organic chemistry the problem arises of the clarification and representation by electronic formulas of the mutual effects of atoms in molecules (electronic effects). Unfortunately, it has not so far been possible to arrive at any conclusive results in this connection. The treatment, on the basis of electronic theories, of the vast amount of experimental material on the mutual influences of atoms and atomic groupings with reference to the role of the reactant and the external conditions, represents an important task of organic chemistry, and constitutes a further broadening of Butlerov's theory of chemical structure.

The existing symbolism, i.e., the method of representation on paper of the order of chemical linking or the recording of the formula of a molecule in a plane or in space is a matter of convention.

There also is a need to work out a more expressive symbolism for the representation of the mutual influences of atoms as a first stage in the development of the electronic theory on the basis of the change in density of the electron cloud. The study of the physical characteristics as a supplement to that of the chemical characteristics would also throw light on this aspect of molecular characteristics.

4. The Value of Butlerov's Experimental Investigations

Butlerov was responsible for a great number of notable experimental studies [27] which have long been finding extensive application in science and technology and have been followed up in various directions by chemists in other countries. These investigations are so well known that it is unnecessary to detail them. We may single out for special mention his investigations on the synthesis of isomers of saturated and olefinic hydrocarbons and of monohydric alcohols (especially trimethylcarbinol and other tertiary alcohols). Well-known are his studies on isomeric transformations (the pinacolin rearrangement, etc.).

The synthesis, worked out in detail, of tertiary alcohols by the organozinc method was the start of the fruitful organozinc syntheses of saturated alcohols (A. M. Zaitsev, E. E. Wagner, V. E. Tishchenko and others) and of unsaturated alcohols (Zaitsev alcohols), of hydroxy acids (the Reformatsky synthesis) and of other classes of organic compounds. We know that these organozinc syntheses form the basis of the well-known organomagnesium synthesis which has superseded the organozinc synthesis. In these, just as in other investigations, Butlerov thoroughly investigated the mechanism of the reactions.

His investigations on olefinic hydrocarbons are of considerable importance in science and industry. Previously, little known, Butlerov's work led to this group of compounds finding extensive application. Butlerov developed many addition reactions of olefinic hydrocarbons. He conclusively established the structure of ethylene; in this research he was greatly aided by his synthesis of ethylene when attempting to prepare a free radical (methylene) from methylene iodide.

These studies were linked with his greatest discoveries which related to the synthesis of polymeric formaldehyde and the synthesis therefrom of monoses by the action of lime water. To Butlerov actually belongs the credit of the first synthesis of sugars. This research served for clarification of the structural formula of monoses. Of special significance is the fact that on the basis of this sugar synthesis it was possible to account for the assimilation of carbon dioxide and water in the green parts of plants with formation of starch. Many very important substances, first prepared by Butlerov, are now manufactured in our factories and throughout the world in quantities of many thousands of tons and are valuable products both in themselves and as starting materials for many chemical derivatives (formaldehyde, urotropine, isobutene, diisobutene, etc.). Butlerov reactions form the basis of industrial organic syntheses.

Butlerov's studies on the synthesis of polymeric formaldehyde, the importance of the Butlerov synthesis of monoses for the understanding of the formation of starch in nature, his notable investigations of stepwise

polymerization of isobutene, which was the precursor of modern syntheses of polyvinyl compounds and of numerous synthetic rubbers (but no longer by a stepwise mechanism but by chain, radical and ionic mechanisms)—all this justifies us in considering Butlerov to be the founder of the science of high-molecular compounds.

The chemistry of high-molecular compounds, developed on the basis of Butlerov's theory of chemical structure, is also much indebted to Butlerov's other investigations, which gave great impetus to the brilliant development of organic synthesis.

The Butlerov school of chemical science, which includes the names of many famous Russian chemists, has left a permanent mark on the development of chemistry in our land.

Chemists of the USSR, the scientific progeny of Butlerov, true followers of Butlerov, surrounded by the all-embracing solicitude of the Communist Party and the Soviet Government, tirelessly work for the glory of the peoples of the USSR by increasing the scientific wealth created by Butlerov and his pupils.

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THE INTERACTION OF NITRATES AND NITRITES OF METALS OF THE FIRST AND SECOND GROUPS OF THE PERIODIC SYSTEM IN MELTS

VIII. INVESTIGATION OF THE TERNARY SYSTEM OF NITRATES OF SILVER, POTASSIUM AND CADMIUM

P. I. Protsenko

Earlier investigations [1, 2, 3] had shown that nitrates of metals of the first group of Mendeleev's periodic system do not behave identically when reacted with nitrates of cadmium in melts. Thus, the nitrates of lithium and sodium do not enter into chemical reaction with cadmium nitrate but form eutectic mixtures with them. On the other hand, the nitrates of potassium and rubidium manifest a marked tendency to form complexes with cadmium nitrate and form the chemical compounds: $Cd(NO_3)_2 \cdot 2KNO_3$ and $Cd(NO_3)_2 \cdot 2RbNO_3$.

The formation of the above complexes is readily explained on the basis of ionic polarizability. The coefficients of polarizability of cations of lithium and sodium are relatively small (0.029 for the first and 0.187 for the second), whereas those of cations of potassium and rubidium are many times larger (0.828 and 1.49 respectively [4]).

The dipoles formed under the action of their own electromagnetic fields in the molecules of potassium and rubidium nitrates on the one hand and in the cadmium nitrate molecule on the other hand, bring about an orientation corresponding to their poles, in consequence of which the above-mentioned chemical compounds are formed.

On reacting cadmium nitrate with silver nitrate we can expect, in view of the polarizability of the silver ion associated with its position in the periodic system, that chemical reaction would also take place between the components.

In this paper we present experimental material which confirms that the interaction of silver nitrate with cadmium nitrate in melts containing various concentrations of components does actually lead to a chemical compound $Cd(NO_3)_2 \cdot 2AgNO_3$, analogous in composition to the compounds of potassium and rubidium nitrates with cadmium nitrate, the new compound is found to be stable (as will be shown below) even in presence of other components.

EXPERIMENTAL

Binary Systems. We have already described [3] the component side of the triangle of the system potassium nitrate – cadmium nitrate. The binary system potassium nitrate – silver nitrate has been investigated by Palkin [5] and by Ussow [6] (Fig. 1, I). Our own study of this system confirmed its general character. The components of the system react with one another and form the chemical compound $AgNO_3 \cdot KNO_3$. The binary system cadmium nitrate – silver nitrate is here investigated for the first time. The phase diagram of this system has three crystallization branches: cadmium nitrate, the compound $Cd(NO_3)_2 \cdot 2AgNO_3$ and silver nitrate. Corresponding to the maximum on the melting point curve is a melting point of 155°. The system was investigated over the range of 100 to 25% silver nitrate; at lower contents of the latter the cadmium nitrate decomposes (Fig. 1, II).

Ternary System. According to the literature sources of which we are aware, no previous study has been made of the ternary system of the nitrates of cadmium, potassium and silver.

The liquidus surface of the ternary system was investigated in 17 sections whose character and direction are shown in Fig. 2.

The melting points at the transition points of the phase diagrams of all the sections as well as the corresponding qualitative and quantitative compositions of the components are set forth in the table.

Melting Points at the Transition Points of the Ternary System and the Composition of the Components

No. of section	Equimolar percentages			Melting point at transition points
	$Cd(NO_3)_2$	KNO_3	$AgNO_3$	
I a*	58	36	6	153
I b*	36.5	59.5	4	166
II a	55	31	14	141
II b	33.5	57.5	9	158
III a	52.2	25.5	22.3	123
III b	31	55.5	13.5	147
IV a	50.2	23	26.8	115
IV b	29	55	16	146
V a	48	20	32	128
V b	45	25	30	125
V c*	27.5	54	18.5	146
VI a	46.5	15	38.5	137
VI b	39.5	28.5	32	128
VI c	25.5	53.5	21	141
VII a	49	5.5	45.5	139
VII b	41.5	4.5	54	150
VIII a	47.5	8.5	44	138
VIII b	41	7.5	51.5	150
IX a	48.5	15	36.5	132
IX b	39.5	13	47.5	149
X a	55	30	15	140
X b	45.5	24.5	30	125
X c	29	31	40	139
XI	27.3	33.7	39	132
XII a	12	40.5	47.5	124
XII b	10.5	48.5	41	128
XIII a	22.5	37.5	40	129
XIII b	18	50	32	132
XIV	36	29	35	129
XV	30.2	55.5	14.3	150
XVI a	7.6	40.5	51.7	124
XVI b	7	47.5	45.5	129
XVII a	3	46.7	50.3	131
XVII b	10.5	43	46.5	126

a* —composition and melting point of the first transition points; b* and c* —ditto of the second and third transition points respectively.

The phase diagrams of all the sections with indication of composition of starting mixtures, the course of the sections and the melting point at the transition points are shown in Figs. 3, 4, 5, 6, and 7.

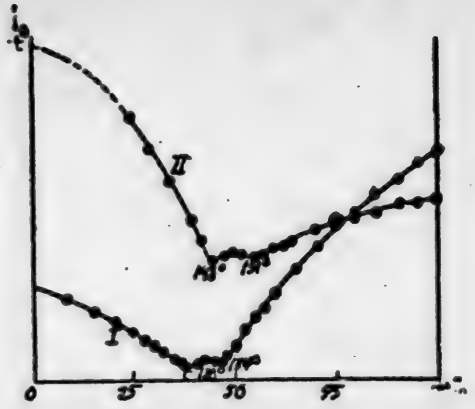

Fig. 1. Binary systems: I) $AgNO_3-KNO_3$, II) $Cd(NO_3)_2-AgNO_3$.

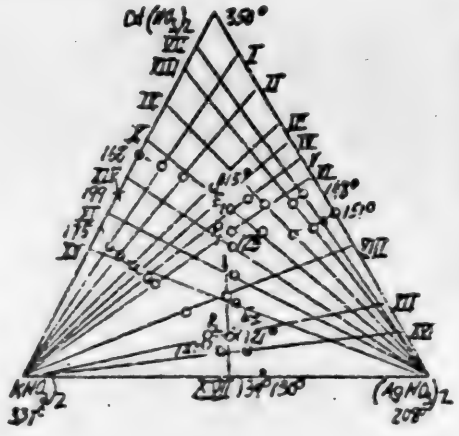

Fig. 2. Course of sections in the ternary system.

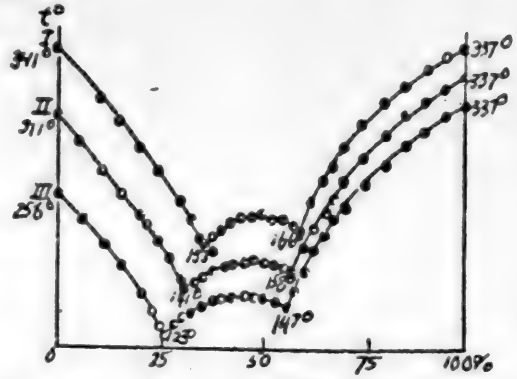

Fig. 3. Ternary sections: I) 90% $Cd(NO_3)_2$ + 10% $AgNO_3$, II) 80% $Cd(NO_3)_2$ + 20% $AgNO_3$, III) 70% $Cd(NO_3)_2$ + 30% $AgNO_3$ in the direction to KNO_3.

The experimental data for the ternary system as a whole are generalized in the projection of the isotherms of the three-dimensional phase diagram (Fig. 8).

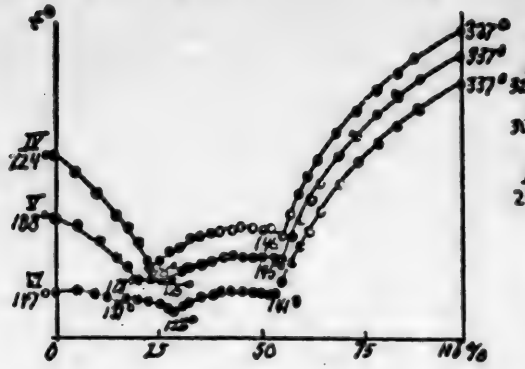

Fig. 4. Ternary sections: IV) 65% $Cd(NO_3)_2$ + 35% $AgNO_3$; V) 60% $Cd(NO_3)_2$ + 40% $AgNO_3$; VI) 55% $Cd(NO_3)_2$ + + 45% $AgNO_3$ in the direction to KNO_3.

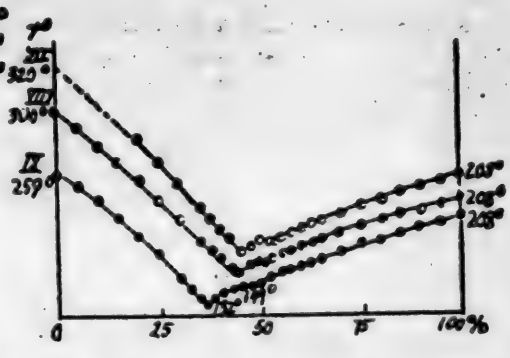

Fig. 5. Ternary sections: VII) 90% $Cd(NO_3)_2$ + + 10% KNO_3; VIII) 85% $Cd(NO_3)_2$ + 15% KNO_3; IX) 75% $Cd(NO_3)_2$ + 25% KNO_3 in the direction to $AgNO_3$.

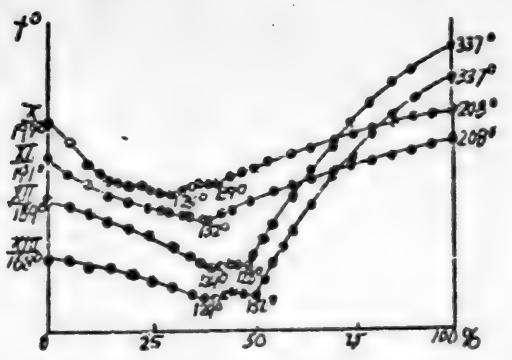

Fig. 6. Ternary Sections: X) 65% $Cd(NO_3)_2$ + + 35% KNO_3; XI) 45% $Cd(NO_3)_2$ + 55% KNO_3 in the direction to $AgNO_2$; XII) 80% $AgNO_3$ + 20% $Cd(NO_3)_2$; XIII) 65% $AgNO_3$ + 35% $Cd(NO_3)_2$ in the direction to KNO_3

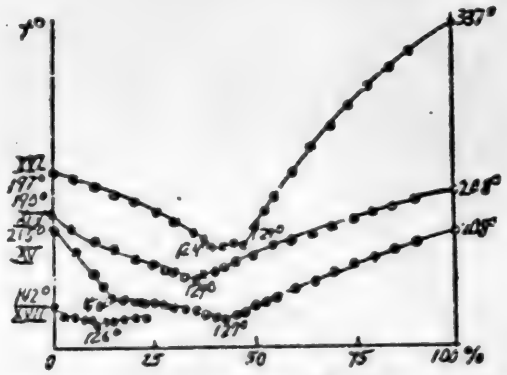

Fig. 7. XIV) 55% $Cd(NO_3)_2$ + 45% KNO_3 → $AgNO_3$; XV) 35% $Cd(NO_3)_2$ + 65% KNO_3 → $AgNO_3$; XVI) 87.5% $AgNO_3$ + 12.5% $Cd(NO_3)_2$ → KNO_3; XVII) 52% $AgNO_3$ + 48% KNO_3 → $Cd(NO_3)_2$

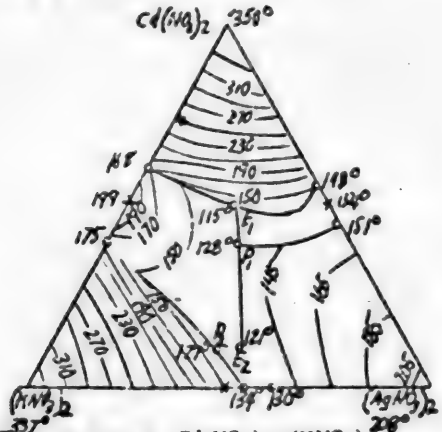

Fig. 8. Ternary system: $Cd(NO_3)_2$–$(KNO_3)_2$–$(AgNO_3)_2$

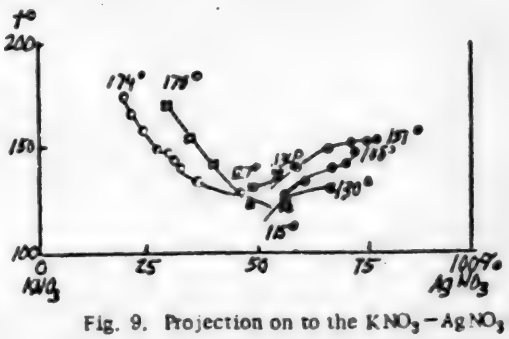

Fig. 9. Projection on to the KNO_3–$AgNO_3$ side.

The ternary system of the nitrates of cadmium, potassium and silver is a complex system. Its distinguishing feature is that pairs of its components: $Cd(NO_3)_2-KNO_3$, $Cd(NO_3)_2-AgNO_3$ and KNO_3-AgNO_3 react chemically and form the above-noted chemical compounds: $Cd(NO_3)_2 \cdot 2KNO_3$, $Cd(NO_3)_2 \cdot 2AgNO_3$ and $KNO_3 \cdot AgNO_3$.

As was to be expected, separate fields of crystallization corresponding to each chemical compound appear on the liquidus surface of the ternary system (Fig. 8). In all there are six fields of crystallization in the system: cadmium nitrate, constituting 23.36% of the whole area of the triangle; potassium nitrate—22.24%; silver nitrate—28.07%; the chemical compound $Cd(NO_3)_2 \cdot 2KNO_3$—20.29%; the chemical compound $Cd(NO_3)_2 \cdot 2AgNO_3$—4.5%; and the incongruent chemical compound $KNO_3 \cdot AgNO_3$—1.6%.

The presence on the liquidus surface of the fields of crystallization of the above-mentioned chemical compounds also confirms their formation inside the ternary system in presence of other components. The quite considerable area of crystallization of the chemical compound $Cd(NO_3)_2 \cdot 2KNO_3$, nearly equal to the areas of crystallization of the pure components—demonstrates its stability.

The ternary system has two eutectic points. The first, E_1, has the composition: 23% potassium nitrate, 50.2% cadmium nitrate, 26.8% silver nitrate; its melting point is 115°. The second, E_2, has the composition: 10.5% cadmium nitrate, 48% silver nitrate and 41.5% potassium nitrate; its melting point is 121°. There are also two peritectic points: P_1 with the composition 28.5% potassium nitrate, 39.5% cadmium nitrate and 32% silver nitrate (melting point 128°); P_2 with 10% cadmium nitrate, 42% silver nitrate and 48% potassium nitrate (melting point 127°).

The orthogonal projection of the courses of crystallization onto the potassium nitrate—silver nitrate side is shown in Fig. 9.

SUMMARY

1. A study was made of the ternary system of the nitrates of cadmium, potassium and silver by the visual-polythermic method of physicochemical analysis; the system was found to be a complex one with four ternary points and six fields of crystallization.

2. A definite chemical reaction is shown to take place between the nitrates of cadmium and silver in melts and the formation was established of the chemical compound $Cd(NO_3)_2 \cdot 2AgNO_3$, melting at 165°.

3. It was shown that chemical interaction between the nitrates of cadmium and the nitrates of potassium and silver in melts takes place not only when in pairs but also within the ternary system; this is confirmed by the existence of the respective fields of crystallization.

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THE PREPARATION OF SILICOMOLYBDIC ACID FROM MOLYBDENUM TRIOXIDE AND SILICIC ACID

E. A. Nikitina, G. N. Pyatnitskaya and I. I. Angelov

The preparation of silicomolybdic acid with purification of the preparation via the etherate was proposed in a paper by one of us [1]. Although it was possible by the proposed method to obtain a pure heteropoly acid, working with such a volatile solvent as ether creates definite complications. We therefore set ourselves the task of developing a method of preparation of silicomolybdic acid which would not involve extraction with ether.

The method involved essentially a reaction between molybdenum trioxide and silicic acid in presence of water as first suggested by E. A. Nikitina [1]:

$$12MoO_3 + H_2SiO_3 + nH_2O \rightleftharpoons H_8[Si(Mo_2O_7)_6].$$

Since the possibility of synthesis of the heteropoly acid from H_2SiO_3 and MoO_3 had already been established, our problem was to make a close study of the conditions in which the above-indicated process of complex formation could be realized.

The molybdenum trioxide needed for the preparation of silicomolybdic acid was obtained in the conditions described in one of our previous papers [2].

In a first series of experiments we conducted the reaction with stoichiometric quantities of MoO_3 and H_2SiO_3; heating of the reaction mixture at 90-95° was continued for 16 hours; the volume of water was kept constant by periodic addition of fresh water; all the experiments were performed with constant stirring (Table 1).

TABLE 1

Preparation of Silicomolybdic Acid with Calculated Amounts of Molybdenum Trioxide and Silicic Acid with a 1:6 Ratio Between MoO_3 and SiO_2

No. of Experiment	Taken for synthesis (in g)		H_2O (in liters)	Duration of heating (hrs)	Sp. gr. of the obtained solution of heteropoly acid at 15°	Amt. of silicomolybdic acid obtained		Yield of MoO_3 (%)	
	MoO_3	H_2SiO_3 calculated as SiO_2				hydrated (in g)	anhydrous (in g)	on the MoO_3 taken	on the reacted MoO_3
1	500	18	3	14	1.06	144	108	20.4	63
2	250	9	1.5	14	1.06	58	44	16.6	73
3	250	9	1.5	18	1.06	66	50	19.6	83

It is seen from Table 1 that the average yield of silicomolybdic acid, calculated on the reacted molybdenum trioxide, is 73% of the calculated yield; but the yield calculated on the molybdenum trioxide taken in the reaction is low and has a mean value of 18.8% for a single boil.

In the following series of experiments it was required to observe the effect of increasing concentration of silicic acid on the degree of utilization of the molybdenum trioxide during the process of formation of the heteropoly acid; the amount of water was the same as in the first series of experiments. Results are set forth in Table 2.

The experimental results show that an increase in the silicic acid concentration raises the amount of molybdenum trioxide utilized in the reaction of complex formation, due to which the yield of heteropoly acid is also appreciably increased.

Table 2

Synthesis of Silicomolybdic Acid Using Increased Concentration of Silicic Acid (Duration of Heating 16 Hours)

No. of Experiment	Taken for synthesis		H_2O (liters)	MoO_3/SiO_2 ratio	Amount of silicic acid obtained (in g)		Yield on MoO_3 (%)	
	MoO_3 (in g)	H_2SiO_3 calculated as SiO_2 with excess (in %) of			hydrated (in g)	anhydrous (in g)	taken	reacted
1	350	50	3	1 : 8.5	80	60	17	73
2	100	100	0.8	1 : 8	22	—	20	—
3	500	500	4	1 : 8	260	200	37.7	100
4	200	500	2	1 : 10	90	70	33	87

A study was also made of the effect of change of dilution on the reaction of formation of the heteropoly acid.

In a first experiment the proportions of molybdenum trioxide and silicic acid were in accordance with the equation; the volume of water was reduced to 150 ml. The yield of silicomolybdic acid was 10% on the molybdenum trioxide taken for the reaction; the ratio between MoO_3 taken and H_2O was 1:1.4. In the second experiment, keeping the amounts of starting substances the same, the water was increased to give a MoO_3/H_2O ratio of 1:55; this raised the yield of silicomolybdic acid, reckoned on the MoO_3 taken, to 16%. Further experiments were therefore performed with increased volumes of water; at the same time the amount of silicic acid was increased in accordance with the results of the second series of experiments.

This change in the experimental conditions increased the utilization of the molybdenum trioxide taken in the reaction to 50-80%. Results are set forth in Table 3.

Table 3

Preparation of Silicomolybdic Acid in Dependence on the Degree of Dilution and the Concentration of Silicic Acid

No. of Experiment	Taken for synthesis		Excess SiO_2 (%)	H_2O (in l)	MoO_3/H_2O ratio	Duration of heating (hrs.)	Amount of silicic acid obtained (g)		Yield on MoO_3 (%)	
	MoO_3 (in g)	H_2SiO_3 calculated as SiO_2 (in g)					Hydrated	anhydrous	On MoO_3 taken	On reacted MoO_3
1	95	13	400	1.8	1:18	19	70	62	29.9	8
2	100	20	550	2.7	1:27	16	110	85	80	100
3	200	40	550	3.5	1:17	16	137	102	50	63

Having established the effect of dilution and of increased silicic acid concentration on the process of complex formation, we directed our attention to the effect of the duration of heating of the reaction mixture on the yield of heteropoly acid.

For this purpose we performed experiments with less lengthy (up to 8 hours) heating of the reaction mixture. These were performed side by side with control experiments in which the duration of boiling was 16 hours.

Results of these runs are set forth in Table 4.

TABLE 4

Effect of Duration of Boiling on the Yield of Silicomolybdic Acid: 500% Excess of H_2SiO_3 Reckoned as SiO_2

No. of Experiment	MoO_3: H_2O	Yield on MoO_3 (%)		Experiment		Duration of boiling (hours)
		MoO_3 taken	Reacted MoO_3			
1	1:18	40	75	Actual		8
2	1:18	49.9	84		Control	16
3	1:27	42	85	Actual		8
4	1:27	80	100		Control	16

These experiments show that prolongation of heating increases the participation of molybdenum trioxide in the reaction of complex formation and thereby raises the yield of silicomolybdic acid.

The foregoing data show that complete conversion of molybdenum trioxide to silicomolybdic acid is never attained in the reaction between MoO_3 and SiO_2. In different batches varying amounts of MoO_3 remain unreacted; in our experiments the amount of reacted MoO_3 ranged from 12 to 80%.

An increased percentage of MoO_3 only enters into reaction when using a large excess (550%) SiO_2 and highly diluted solution (1:25).

High dilutions, however, greatly prolong the period of evaporation of the solutions of heteropoly acids. We therefore compromised with a mean dilution of 1:15 to 1:17 and the use of a 500% excess of SiO_2 over the amount calculated from the equation.

The residue of unreacted MoO_3 and H_2SiO_3 is used again by heating with a fresh portion of water; in so doing a favorable influence of excess H_2SiO_3, dilution of solution and duration of reaction on the degree of utilization of MoO_3 is again noted. The results of the investigation are set forth in Table 5.

TABLE 5

Results of Reheating with Water of Residual MoO_3 and H_2SiO_3 from a First Synthesis

No. of Experiment	Dry slurry taken (g)	Its content of MoO_3 (%)	H_2O taken (liters)	H_2SiO_3 added (calculated as SiO_2 (g)	Amount of hydrated silicomolybdic acid obtained (g)	Residue of dry slurry (g)
1	350	89	0.5	—	35	320
2	200	96.5	1.5	30	58	127
3	267	89	2.5	20	110	289

We see from Table 5 that the nonreacted residues of MoO_3 and H_2SiO_3 may be utilized as starting materials by adding a fresh amount of silicic acid since the dried H_2SiO_3 loses its reactivity.

Crystallization of silicomolybdic acid. The preparations of diluted solutions of silicomolybdic acid (sp. gr. 1.02-1.06) are evaporated on a water bath at 70°. Due to the high solubility of silicomolybdic acid in water, the evaporation is continued until the volume is 1/5 to 1/6 of the original.

Silicomolybdic acid separates from solution in the form of a greenish-yellow crystalline mass. The great evaporation of the solutions leads to the crystallization of a dense mass which is detached with difficulty from the walls of the crystallizer and is quite free from mother liquor. In the process of evaporation (open beaker) a slight reduction of the heteropoly anion is observed; this is counteracted by the addition of a few drops of 3% hydrogen peroxide. Evaporation may also be conducted under reduced pressure; this speeds up the removal of water and minimizes the reduction of the Mo^{VI} of the heteropoly anion.

TABLE 6

Analyses of Silicomolybdic Acid and Quality of Raw Materials

No of Preparation	Chemical compounds	MoO_3 without washing free from alkali; H_2SiO_3 contains 1% Na_2O	MoO_3 without alkali salts; H_2SiO_3 contains 0.5% Na_2O	MoO_3 free from alkalies; H_2SiO_3 contains 0.5% Na_2O. Distilled water (%)	Content of anhydrous acid calculated according to the formula
		Tap water (%)			
1	MoO_3	93.47	95.8	95.6	92.9
2	SiO_2	3.13	3.5	3.86	3
3	Na_2O	3.4	0.7	0.35	—
4	$MoO_3 \cdot SiO_2$	29.3	27.3	24.9	—

Balance of starting materials. In order to check the composition of the slurry, we carried out its analysis by distilling off the MoO_3 in the form of $MoO_3 \cdot 2HCl$ hydrochlorination of a weighed amount was effected at

a temperature of about 600°. In all the analyses the amount of components (SiO_2 and MoO_3) closely agreed with the calculated amount of reacted starting substances.

Weight of slurry dried at 110°: 325 g. Analysis: SiO_2 11%, MoO_3 89%.

Raw Materials. In our experiments we made use of ammonium molybdate "pure" and "pure for analysis". The MoO_3 prepared from "pure" ammonium molybdate contained from 1 to 1.7% alkali salts (reckoned as Na_2O). The MoO_3 was freed from traces of alkali metals by washing with hot distilled water (80-90°) until a colloidal solution started to form. Washing H_2SiO_3, which has been precipitated with nitric or hydrochloric acid, until it gives a negative reaction for Cl^- or NO_3^- is a lengthy operation. The lowest Na_2O content found after washing of freshly precipitated H_2SiO_3 was 0.5% (calculated on the SiO_2). Employment of such a silicic acid leads to a final product containing alkali salts.

Precipitation of H_2SiO_3 with carbon dioxide gives a silicic acid which is readily washed and which exhibits good reactivity. The content of non-volatile residue of alkali salts in the so-prepared H_2SiO_3 is 0.025-0.03%. Silicomolybdic acid prepared by crystallization from aqueous solutions was examined by us for its content of MoO_3, SiO_2 and alkali salts (reckoned as Na_2O); loss of water was also determined at 100° and on calcination; the analytical results for samples of the heteropoly acid are set forth in Table 6.

The obtained preparations consist of saturated silicomolybdic acid.

The above data show that the quality of the obtained silicomolybdic acid depends on the purity of the starting materials.

The water content of the prepared samples of silicomolybdic acid was determined.

Losses of water at 100° amounted to 20.0, 20.3, 16.8, and 17%. The corresponding losses of water on calcination were 4.0, 2.2, 6.4, and 5.0%.

SUMMARY

1. For the first time a method of preparation of silicomolybdic acid not using ether has been developed.

2. Conditions necessary for obtaining the heteropoly acid are: 400-500% excess of silica, a reaction period of 16 hours and a volume of water equal to 8 liters per 500 g MoO_3.

3. The yield of silicomolybdic acid in these conditions is 80-90% reckoned on the MoO_3 entering into reaction.

4. 50% of the molybdenum trioxide taken enters into reaction. The unreacted MoO_3 is reused as starting material after determination of its MoO_3 content.

5. The starting materials for this method must be of a high degree of purity since it is impossible in practice to free the heteropoly acid from water-soluble impurities by crystallization.

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POLAROGRAPHIC INVESTIGATION OF THE HYDROGENATION PROCESS. I.

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An examination of the methods used by various authors for studying the behavior of unsaturated compounds in the course of catalytic hydrogenation shows that we can subdivide them into two groups. To the first group belong methods based on the establishment of the velocities of hydrogenation of individual unsaturated compounds and on the comparison of these velocities for a series of chemically related compounds.

In the majority of cases the velocity of saturation of unsaturated compounds is measured by the volume of hydrogen which combines in unit time, or by the time required for saturation of a specified quantity of substance expressed as moles, or by the time required for addition of a specified volume of hydrogen to a given quantity of the compound, or, finally, the velocity of saturation is measured from the rate of change of some physical constant of the substance, such as the refractive index, the rotatory power, etc..

A number of authors [1-10] have employed the technique of comparing the velocities of saturation of pure compounds to draw conclusions about the effect of the structure of the molecules on the activity of the multiple bond in the process of catalytic hydrogenation. Other authors [11, 12], by hydrogenating mixtures of pure unsaturated compounds with one and the same standard substance, have compared the so-obtained partition coefficients of hydrogen and have established the effect of structural peculiarities of molecules on the reactivity of the double bond.

It has been found, however, that comparison of the rates of saturation of pure compounds, or determination of the coefficients of distribution of hydrogen between pure unsaturated compounds and the standard substance, do not permit us to draw conclusions about the behavior of these unsaturated compounds in mixtures.

The second group of methods of study of the behavior of unsaturated compounds during the hydrogenation process includes the methods of joint hydrogenation of two competing substances, of hydrogenation of binary mixtures with the aim of direct establishment of the order of hydrogenation of the components of the mixture. We must bear the following facts in mind: 1) In the vast majority of cases the experiments were run with small amounts of material (1/200 to 1/100 mole); 2) if the starting mixture contains two components then the saturation process will lead to at least two hydrogenation products so that the binary mixture is changed into a quaternary mixture; 3) the quantitative separation of compounds, especially when they are similar in functional character, is extraordinarily difficult and in the majority of cases impossible. In order to be able to follow the whole course of the process, it would be desirable to withdraw small samples of reaction mixture at definite intervals of time and to analyze them. But if, say, one-tenth of the mixture is to be withdrawn each time, this would correspond to 1/2000 to 1/1000 mole. It would be a very difficult problem to separate such an amount into the four components for the purpose of establishing the content of each in the mixture. Very rarely, therefore, is the attempt made to effect direct analysis of a mixture at different stages of hydrogenation, and even as a rule for the purpose of evaluating the course of the process of saturation of binary mixtures, recourse is had to indirect methods. The most important of the indirect methods is that developed by S. V. Lebedev [13] which is based on the study of hydrogenation curves.

Such a method, however, does not permit the study of intermediate processes, i.e. with a not strictly maintained selectivity; in the course of the process one component of the mixture is preferentially saturated; at the same time the other component undergoes saturation although at a much lower velocity. The degree of selectivity of the process may vary widely and the hydrogenation curves do not permit us to determine the degree of selectivity.

Other workers apart from S. V. Lebedev who studied the course of hydrogenation of binary mixtures of diolefinic and acetylenic compounds on the basis of the character of the hydrogenation curves were Dupont [14], Armstrong and Hilditch [15] and Yu S. Zalkind [16].

The marked inadequacy of the information supplied by the hydrogenation curves prompted the first investigators of problems of selectivity of hydrogenation to resort to analysis of the mixtures, using the method of interrupted hydrogenation. This method consists essentially in interrupting the hydrogenation of an equimolecular mixture of two unsaturated compounds when 50% of the theoretical amount of hydrogen has been absorbed and

and then analyzing the mixture as a whole; on the basis of the results of this analysis, conclusions are drawn about the presence or absence of selectivity and about the degree of selectivity of the process.

Of the numerous authors who utilized the method of interrupted hydrogenation, we may mention Vavon [17], Bourguel [18], Yu. S. Zalkind [16, 19], B. A. Kazansky [20] and M. I. Ushakov [9].

Different authors used different methods of analysis of the reaction mixture [21]. In all cases the procedure is quite complicated; the main defect of the method is that it characterizes the rate of the process not throughout its entire course, but only at one determined moment.

It is therefore natural to search for a method which would permit the course of the process to be followed at any rate at a few points. The obvious plan is to effect direct or indirect analysis of samples withdrawn from the reaction mixture at intervals throughout the process.

Many attempts to develop a procedure along these lines have been made. We may refer to the work of Vavon [22] who followed the course of hydrogenation of limonene and carvone by withdrawing samples from the reaction mixture at intervals and measuring the angle of rotation of the plane of polarization of light.

In the study of the process of hydrogenation of fats with the objective of establishing its selectivity, Kaufmann [23] and later Zinovyev [24] successfully applied the method of determination of the iodine and thiocyanogen numbers.

V. V. Ipatyev [25] hydrogenated a mixture of allyl alcohol and oleic acid and withdrew samples over definite intervals of time; he determined the amount of stearic acid formed by precipitation with magnesium acetate and the total amount of unsaturated compounds remaining in solution from the amount of iodine chloride absorbed by them. A slightly modified procedure was employed by I. F. Bogdanov and E. I. Bashkirova [26].

Performance of an experiment in the apparatus used in the above-cited investigations [24, 26] necessitated relatively large amounts of unsaturated compounds, in addition to which the procedure for analysis of the mixtures was rather complicated. We therefore reached the following conclusions:

1. Study of the course of the hydrogenation of binary mixtures from the saturation curves (S. V. Lebedev) only gives an approximate conception of the character of the process.

2. The method of interrupted hydrogenation does not give an idea of the rate of the process throughout its entire course, so that its value is seriously limited.

3. The method of withdrawal of a series of samples in the course of the process is the most interesting and informative in the sense that it permits study of the kinetics of the process. Up to now, however, the proposed methods of analysis of mixtures have been laborious, only applicable to a limited number of materials, and frequently required large amounts of substance.

In seeking for an analytical method of adequate sensitivity and accuracy, speedy and easy in use, enabling operation with very small quantities of substance, and applicable to a fairly wide range of chemical compounds, we decided on the polarographic method.

In the conditions of the investigation we were faced with the following problem: Knowing that two given unsaturated compounds are present in the mixture to be hydrogenated, and knowing also the amount of hydrogen consumed up to the instant of withdrawal of the sample from the vessel, it is desired to determine polarographically how much of each unsaturated compound is left in solution, assuming that the respective saturated compounds do not give polarograms and that their presence does not affect the polarographic behavior of the unsaturated compounds.

This problem can be solved in two ways, depending upon whether both or only one of the unsaturated components of the mixture give polarograms.

In the event that both components of the mixture give definite and separate polarographic waves, the problem is solved by plotting polarograms at different stages of hydrogenation, by measurement of the height of each wave and, insofar as the proportionality coefficient between the diffusion current and the concentration is known, by calculation of the concentration of each component in the solution. In the course of the hydrogenation reaction, either the heights of the waves of both components will gradually decrease but the change will differ for each component in dependence on the degree of selectivity of the process, or both waves will decrease to identical extents at the same time (non-selective process) or the heights will decrease simultaneously, but at different rates (one more quickly than the other—not strictly selective process), or at first only the height of one of the waves will decline and its disappearance will be followed by the start of decline of the other wave (strictly selective process).

In Figure 1 are shown curves obtained by polarographic determination of a series of specimens withdrawn during the hydrogenation of a mixture of maleic and fumaric acids; on these curves the wave at a more positive value of the potential relates to maleic acid; that at a more negative value to fumaric acid. The half-wave potential of maleic acid differs from that of fumaric acid by 0.2 V, which allows of clear demarcation of one wave from the other. Measurements of the height of the waves on the curves gave us the values set forth in Table 1.

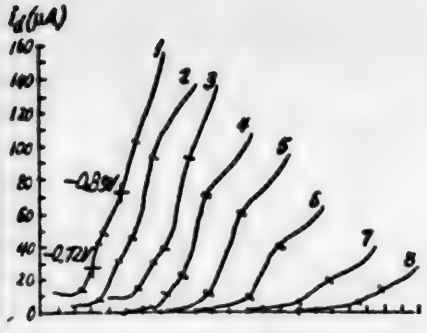

Fig. 1. Polarograms of mixtures of maleic and fumaric acids $\eta = 1/10$. Explanation in text and Table 1.

In the starting solution (specimen no. 1, Table 1) the concentrations of maleic and fumaric acid were taken as equal to:

$$C_m = C_f = 250 \cdot 10^{-6} \text{ mol/liter.}$$

We see from the data of Table 1 that maleic acid is preferentially hydrogenated in comparison with fumaric acid; the selectivity, however, is not strict since at the instant of complete disappearance of maleic acid, the fumaric acid has been partly (only to the extent of 17%) hydrogenated.

In some cases it is useful to obtain information about the concentration of the substance which is being analyzed by applying the so-called method of addition of a standard solution, which ensures greater accuracy of determination, although a longer period is then required for the determination. In the present investigation we resorted to this method in many cases.

When only one of the two components of a mixture forms a polarogram, the change of content of that compound in the course of hydrogenation can be directly determined by measurement of the height of the single wave on the polarograms of withdrawn samples; the change in content of the other component is calculated by the method explained in the example below.

Figure 2 contains a series of polarograms plotted for samples of a solution of an equimolar mixture of fumaric acid and oleic acid which had been subjected to hydrogenation; samples were taken throughout the course of the reaction at intervals corresponding to absorption of each 20-30 ml hydrogen. Only one wave changes on the polarogram — that of fumaric acid oleic acid does not give a polarographic wave. The initial concentration of fumaric acid (as also that of oleic acid) was $250 \cdot 10^{-6}$ mole/l. The heights of the waves of all nine curves in Figure 2 and the corresponding concentrations of fumaric acid are set forth in Table 2.

TABLE 1

No. of samples on curves	Height of wave (mm)		Maleic acid $C \cdot 10^{-6}$	Fumaric acid $C \cdot 10^{-6}$
	Maleic acid	Fumaric acid		
1	405	660	250	250
2	270	660	167	250
3	190	620	117	235
4	120	600	74	227
5	0	545	0	207
6	0	352.5	0	134
7	0	140	0	53
8	0	70	0	26

In the experimental conditions of the experiment which we describe as an example, the saturation of the weighed amounts of fumaric and oleic acids (each 0.005 g mole) should have required 246.2 ml hydrogen (at an air temperature of 14° and a barometric pressure of 727 mm). Such an absorption should correspond to a fall in the concentration of each of the acids, in the solutions diluted for polarographing, from $250 \cdot 10^{-6}$ mole/l to nil. Assuming, for convenience, $1 \cdot 10^{-6}$ mole/l as unit of concentration, we may say that the concentration of each acid in these arbitrary units before the start of hydrogenation was 250 (total 500) and that after completion of hydrogenation it was 0. Hence the fall in concentration for each arbitrary unit corresponds to a hydrogen absorption of $\frac{246.2}{500} = 0.4924$ ml.

The amount of hydrogen absorbed up to the instant of withdrawal of each of the samples is known from the readings of the gas burets; we must, however, introduce a correction into these readings; on withdrawing a sample of solution for analysis, we change each time the absolute weight of unsaturated compounds participating in the reaction. In the experiment we are now considering, the first sample was taken before the start of hydrogenation; samples 2 to 8 were each taken after absorption of 20.0 ml hydrogen; sample 9 was taken after absorption of 29.2 ml hydrogen. The volume of each sample was 2 ml while that of the original solution was 40 ml. The volumes of hydrogen which would have been absorbed by the original amount of material at the instant of withdrawal of the samples are shown in Table 3, from which we see how the volumes were calculated.

TABLE 2

No. of sample and curve	Height of fumaric acid wave	Fumaric acid $C \cdot 10^{-5}$
1	370	250
2	350	236
3	310	209
4	280	189
5	240	162
6	170	115
7	110	74
8	67	45
9	0	0

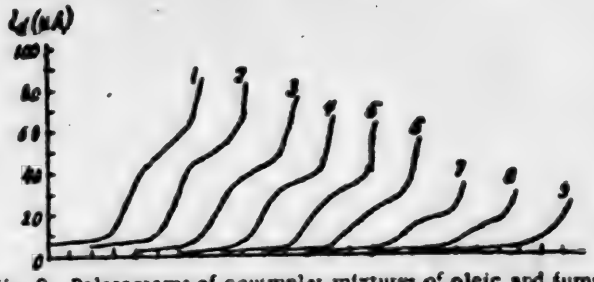

Fig. 2. Polarograms of equimolar mixtures of oleic and fumaric acids. η = 1/10. Explanation in text and Table 2.

Knowing the fall in concentration of fumaric acid at the instant of withdrawal of each sample, we calculate how much hydrogen was consumed in saturating this acid by multiplying the fall in concentration ΔC by 0.4924; the difference between the total absorption and the absorption by fumaric acid corresponds to the absorption of hydrogen by oleic acid; on dividing this difference by 0.4924, we obtain the fall in oleic concentration at the instant of withdrawal of a sample

This calculation is illustrated for a specific example in Table 4.

Consequently, in this case also, when only one of the two unsaturated components forms a polarogram, we still have the possibility of sufficiently accurately tracing the change of concentration of both components in the course of hydrogenation.

On the basis of the foregoing observations, we arrive at the conclusion that polarography enables us to follow the course of joint hydrogenation of two unsaturated compounds either when the respective saturated compounds do not give polarographic waves (as is mostly the case), or when both unsaturated compounds give sharply separated waves, or only one of the two compounds gives a polarographic wave. Experiment showed that by varying the conditions of polarography (the nature of the solvent and the pH) it is nearly always possible to an adequate extent to separate the waves of the two unsaturated compounds or to suppress one of the waves.

TABLE 3

No. of sample	Hydrogen absorbed (in ml)	Vol. of solution (in ml)	Formula for calculation	Total absorption of H_2 (in ml)
1	0	40	—	0
2	20	38	$\frac{20 \cdot 40}{38}$	21.1
3	20	36	$21.1 + \frac{20 \cdot 40}{36}$	43.3
4	20	34	$43.3 + \frac{20 \cdot 40}{34}$	66.8
5	20	32	$66.8 + \frac{20 \cdot 40}{32}$	91.8
6	20	30	$91.8 + \frac{20 \cdot 40}{30}$	118.5
7	20	28	$118.5 + \frac{20 \cdot 40}{28}$	147.1
8	20	26	$147.1 + \frac{20 \cdot 40}{26}$	177.9
9	29.2	24	$177.9 + \frac{29.2 \cdot 40}{24}$	226.5

TABLE 4

No. of sample	Fumaric acid		Total H_2 absorption (ml)	Distribution of H_2 over		Oleic acid	
	$C \cdot 10^{-5}$	$\Delta C \cdot 10^{-5}$		Fumaric acid	Oleic acid	$\Delta C \cdot 10^{-5}$	$C \cdot 10^{-5}$
1	250	0	0	0	0	0	250
2	236	14	21.1	6.9	14.2	29	221
3	209	41	43.3	20.2	23.1	47	203
4	189	61	66.8	30.0	36.8	75	175
5	162	88	91.8	43.3	48.5	98	152
6	115	135	118.5	66.5	52.0	106	144
7	74	176	147.1	86.7	60.4	123	127
8	45	205	177.9	100.9	77.0	156	94
9	0	250	226.5	123.1	103.4	210	40

Consequently the polrrographic method of investigation is only unsuitable in cases when both unsaturated compounds do not give polarograms or when the two waves coincide or have similar reduction potentials in all the conditions of polarogramming.

Our apparatus for carrying out hydrogenations most closely resembled that of S. V. Lebedev [27] and different in minor details.

The hydrogenation vessel is a duck and differs from the normal type in the presence, apart from two openings with taps of which one serves for connecting the hydrogen buret and the other for connection to atmosphere, of a third, small lateral opening which can be tightly closed by means of a tautened rubber cap; this opening is intended for withdrawal of samples during hydrogenation. The duck was rocked 300, 225 and 150 times per minute. Hydrogenation was performed with the catalyst prepared by A. S. Ginzberg's method [28]. Through the sampling opening was introduced a weighed amount of aluminum or nickel powder; the particles of metal were washed off with 5 ml solvent (usually alcohol). Through the same opening with a pipet was introduced, depending on the circumstances, 5 or 10 ml aqueous or alcoholic solution of $PdCl_2$ or Na_2PdCl_4 of predetermined concentration. The opening was then closed with the rubber cap, the duck secured in the frame of the shaker, immersed in a thermostat and connected by a rubber tube with the hydrogen line. The experimental temperature was 25 or 40°. Through the duck was passed 500 ml hydrogen, the tap was closed, and the duck connected to atmosphere; with the help of a medicinal syringe – by means of which the rubber cap is punctured – a solution of 1/200 to 1/100 g/mole of the substances or mixture of substance to be hydrogenated is introduced; with the same syringe is also introduced a small amount of solvent in order to bring the total volume of liquid to 40 ml. After the hydrogen in the buret has been levelled to atmospheric pressure, the shaker is started and reading is started of the amount of absorbed hydrogen every 60 seconds with the help of a timing device.

Samples are withdrawn in the following way: The shaker is stopped, the cap is punctured with the needle of a syringe, 2 ml is aspirated from the duck, and the shaker is again started. The sample is transferred to a vessel from which exactly 1 ml is withdrawn with a pipet, transferred to a moistened filter for separation of the catalyst, and repeatedly washed with the solution serving as the medium for the subsequent polarographic analysis; the volume of the filtrate is made up with the same solution to 25 ml or, more often, to 50 ml.

The first sample is withdrawn before the start of hydrogenation, the subsequent samples are taken off after each 20 ml of absorbed hydrogen.

The polarographic analysis was performed with the A-3 polarograph and with the M-7 visual polarograph. The comparison electrode was a saturated calomel electrode.

SUMMARY

1. For the purpose of investigating the selectivity characteristics in the course of hydrogenation of mixtures of unsaturated compounds, the method of polarographic analysis of samples withdrawn during the hydrogenation is proposed.

2. It is shown that the polarographic method is suitable when both components of the mixture give clearly resolved waves and also when one of the two unsaturated compounds gives a polarographic wave and the other does not give a wave.

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A SYSTEM WITH AN ENCLOSED REGION OF STRATIFICATION

THE RECIPROCAL SOLUBILITY OF HEXAMETHYLENEIMINE AND WATER

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At the present time the general assumption is that the usual form of solubility curve of binary systems is a closed ring [1]. In the majority of systems, however, it is impossible to observe either upper or lower critical points. It is especially rarely that we encounter systems with a lower critical point. This circumstance is usually explained by the onset of crystallization [1]. The few systems with a lower critical temperature which have been studied are characterized by the formation of chemical compounds which (as illustrated by R. V. Mertslin [2] with reference to mixtures of water and some amines) break down into their original constituents on heating so that stratification of the homogeneous solutions takes place. Due to the strong attraction between different types of molecules at low temperatures, the components of chemically interacting binary systems form homogeneous solutions. With rising temperature, the possibility of development of heterogeneous mixtures arises at the same time as decomposition of the associated, solvated or other types of compounds.

We have studied the reciprocal solubility of hexamethyleneimine and water. As had been expected, in the light of the foregoing considerations, notwithstanding the complete reciprocal solubility of the two substances at room temperature [3], a lower critical point was observed in the system hexamethyleneimine–water. We also succeeded in demarcating both branches of the solubility curve and in finding the position of the upper critical point.

EXPERIMENTAL

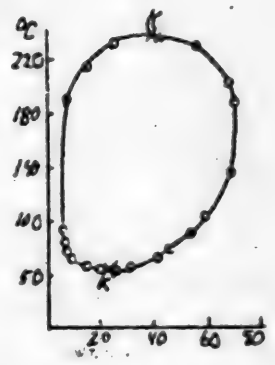
The hexamethyleneimine whose constants had been previously determined [3] was used in the experiments. Solubility was determined by the polythermal method of V. F. Alekseev [4], based on the appearance and disappearance of turbidity on slow heating of mixtures of determined composition in sealed tubes.

TABLE 1

Reciprocal Solubility of Hexamethyleneimine and Water

Temperature (in °)	Content of hexamethyleneimine in mixture (wt. %)	
	in upper layer	in lower layer
66.9°	22.5	22.5
70	36.8	10.0
80	49.6	6.8
90	57.5	5.8
100	62.4	5.7
110	65.5	5.7
120	67.5	5.7
130	68.9	5.7
140-160	70.3	5.7
170	70.3	5.8
180	70.3	6.0
190	70.0	6.8
200••	68.0	9.8
210	62.5	15.5
220	53.0	22.9
228•	39.5	39.5

The curve of reciprocal solubility of hexamethyleneimine and water (see diagram) was plotted on the basis of the experiments performed. Interpolated data are set forth in the table.



Curve of reciprocal solubility of hexamethyleneimine and water. K – critical points.

•Critical temperature.

••On heating above 200° the contents of the tubes turned yellow.

The lower critical temperature (found to be 66.9°) was determined experimentally. Critical opalescence was observed at this temperature. The upper critical temperature is 228° and was obtained by graphical extrapolation by extending the line joining the center of the connecting straight lines up to the point of its intersection with the solubility curve.

Since the system hexamethyleneimine-water has both an upper and a lower critical temperature, both branches of the solubility curve are characterized by the presence of "minimum solubility", i.e. points (or, in our case, sections) above and below which the solubility rises.

SUMMARY

1. It is shown that the system hexamethyleneimine-water possesses both a lower and an upper critical temperature. Corresponding to the lower critical temperature (66.9°) is a mixture containing 22.5 wt. % hexamethyleneimine; corresponding to the upper critical temperature (228°) is one containing 39.5 wt.% hexamethyleneimine.

2. The minimum of solubility of hexamethyleneimine in water occurs at 100-160° and is 5.7%. The minimum solubility of water in hexamethyleneimine is 29.7% and is observed over a very broad temperature range (140-180°).

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MELTING POINTS AND POLYMORPHIC TRANSFORMATIONS OF THE HYDROXIDES OF LITHIUM, SODIUM AND POTASSIUM

V. A. Khitrov, N. N. Khitrova and V. F. Khmelkov

It is usually assumed that the melting point of lithium hydroxide is 445°, that of sodium hydroxide 318.4° and that of potassium hydroxide 360° [1]. Being engaged over a period of years in the study of the interaction of hydroxides of alkali metals with salts in melts, we were naturally forced to pay attention to the purity of our preparations and, in particular, to the purity of the alkalies. We prepared the purest NaOH and KOH, on A. G. Bergman's suggestion, from chemically pure metals (Kahlbaum), in a silver beaker under a glass bell, by the action on these metals of twice-distilled water in an atmosphere of hydrogen followed by dehydration at about 500° in a furnace constantly filled with air from which carbon dioxide and water vapor had been completely removed (by passage through two Tishchenko bottles containing sulfuric acid and three columns filled with small lumps of KOH). Analysis of the NaOH and KOH prepared by this method showed that they contain only traces of moisture and carbonates; their melting points were respectively 322 and 406° [2].

The melting points of the caustic alkalies were measured in a specially designed muffle furnace [2] filled with air free from carbon dioxide and water vapor. Measurement was effected with a nichrome-constantan or gold-platinum thermocouple whose hot junction was directly immersed in the alkali melt. The scale of the millivoltmeter was graduated on the basis of the boiling point of water and the melting point of chemically pure metals (tin, lead and zinc). The alkalies were melted in silver crucibles. The thoroughness of the protection of the alkali melt against the surrounding air in our procedure is evident from the fact that the melting point of the alkali melts remained substantially unchanged even after a residence time of 10 hours in the furnace.

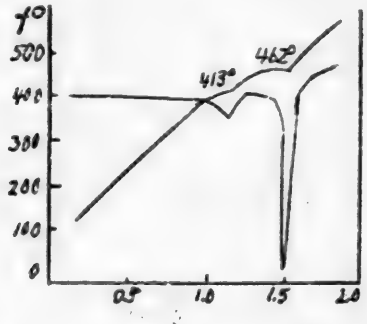

Fig. 1. Heating curve of LiOH

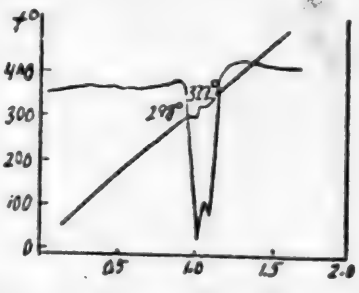

Fig. 2. Heating curve of NaOH

We also obtained good results in the purification of chemically pure hydroxides (Umformer, Merck and Kahlbaum grades) by Sorensen's method [3], involving standing for many days of the saturated aqueous solutions followed by careful dehydration for 6 hours in an atmosphere freed from carbon dioxide and water vapor. Our results were sufficiently good: melting point of NaOH 320-321°; of KOH 403-404°; of LiOH 462-463°. We thought it necessary to check the data for the melting points of the hydroxides of lithium, sodium and potassium against the heating curves of specimens purified by one of the above-mentioned methods. For this purpose we used the pyrometer of N. S. Kurnakov and a differential recorder.

The hot junction of the nichrome-constantan thermocouple was directly immersed in the alkali melt. This thermocouple had been graduated against the boiling point of water and the melting points of chemically pure tin, lead and zinc. The alkali melt was contained in a silver crucible placed in a stout silver block. The alkali was melted in a furnace constantly filled with air from which carbon dioxide and water vapor had been removed. The thermocouple was mounted in the massive silver cover of the crucible. In this set-up the block was rapidly cooled with liquid oxygen contained in an aluminum vessel the air in which was free from carbon dioxide and water vapor. The block was transferred to the furnace and the heating curve was plotted. Programmed temperature

regulation was effected according to the scheme proposed by V. I. Kaurkovsky [4] with the help of a potential regulator for which a thyratron relay served as the impulse element.

The plotted curves (Figs. 1 to 3) confirmed our data and we can now confirm that the melting points are LiOH 462°, NaOH 322° and KOH 406°.

Repeated recordings of the heating curves of the hydroxides of lithium, sodium and potassium also gave information about the number and temperatures of the polymorphic transformations of these compounds. We could establish the presence in LiOH of a polymorphic transformation which, as far as we know, has not previously been reported. Transition of the α-modification of LiOH into the β-form takes place at 413°(Fig. 1).

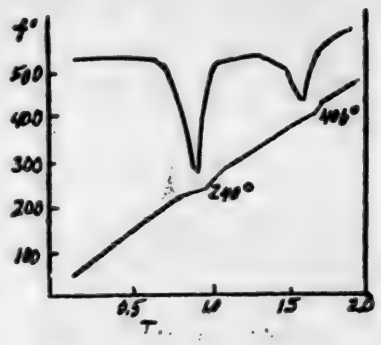

Fig. 3. Heating curve of KOH

The transition from one modification of NaOH into the other occurs at 298°. It is very interesting to note that the endothermic effect of the polymorphic transformation of NaOH is very much larger than the melting effect. This is undoubtedly bound up with the fact that both effects occur at almost identical temperatures (Fig. 2). Contrary to the statement of N. A. Reshetnikov and G. G. Diogenov [5], who found three polymorphic modifications of KOH with transformation temperatures of 268 and 375°, our repeated and highly concordant checks revealed only one extremely marked endothermic effect at 240°, corresponding to the transformation of the α-modification of KOH into its β-form (Fig. 3). As in the case of NaOH, the effect of the polymorphic transformation of KOH was much more conspicuous than the melting effect.

T. A. Polivanova collaborated in the research and the authors extend their thanks to her.

SUMMARY

1. Carefully purified hydroxides of lithium, sodium and potassium have higher melting points than those recorded in the handbook literature.

The following melting points were established by visual and thermographic investigation: lithium hydroxide 462°; sodium hydroxide 322°; potassium hydroxide 406°.

2. The heating curves of the thoroughly purified hydroxides of lithium, sodium and potassium permit the establishment of the number and temperature of the polymorphic transformations of these compounds. For the first time we established the existence of two polymorphic modifications of LiOH with a transformation temperature of 413°. The temperatures of polymorphic transformations of sodium and potassium hydroxides are respectively 298 and 240°.

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* See Consultants Bureau Translation, page 743.

CATALYTIC TRANSFORMATIONS OF HYDROCARBONS

RMATIONS OF DIPHENYLETHANE AND DITOLYLETHANE

Dobryansky, L. A. Ponomarev and L. D. Dybkin

k on the transformation of diphenylmethane [1], studies were made of the decomposi-tolylethane. As we know, the first of these hydrocarbons forms toluene and complex lysis. In precisely the same way ditolylethane forms dimethylbenzene and anal- However, whereas diphenylethane forms only toluene, ditolylethane gives, apart benzene, an appreciable amount of toluene. This reaction also occurs appreciably th anhydrous aluminum chloride, the action of the latter being quite similar to that en expected that on heating with aluminosilicate catalyst the indicated course of marked.

EXPERIMENTAL

esized from benzene and dichloroethane in presence of aluminum chloride. The a large excess of benzene (100 parts dichloroethane, 900 parts benzene and 6 parts n of reaction of 6 hours, and heating on the water bath to 90° (at the end of the re- e yield was about 70%.

on precisely similar lines; the yield rose to 80% of lethane was purified by on from alcohol (m.p. d by distillation; the 290- he ortho-isomer melted at nly the meta-isomer is a e with a viscosity at 20° 9677, n_D^{20} 1.5750. Judging c acids obtained on oxida- te, this substance is a mix- % para-isomer.

nts on the transformation ed in standard conditions, ted gumbrin as catalyst, effected over a burner periods of time. The tem- ermometer immersed in ration of a determined nd a sample of the liquid benzene content.

wing yields of benzene in eating (Table 1).

TABLE 1

Yield of Benzene in the Transformation of Diphenylethane

Temp. (in °C)	Duration of heating (in hours)	Yield of Benzene (in %)
170	4	0.5
	9	2.1
	10	2.3
	20	2.9
	30	3.1
	40	3.1
180	1.5	1.2
	4	2.3
	8	3.6
	10	3.8
	20	4.6
	35	4.7
190	1	3.8
	4	6.0
	7	9.7
	10	12.2
	15	14.5
	18	15.0
	26	15.0

obtained: d_4^{20} 0.8790, n (4 mm) of the higher 200-260° and 270-290°. The latter fraction markedly predominated. Analysis ctions showed that it consists of undecomposed diphenylethane contaminated with

on.

1.279. Diphenethylbenzene $C_{22}H_{22}$. Calculated %: C 92.30; H 7.70; M 286.

Oxidation of the second fraction with potassium permanganate gave (from 5 g hydrocarbon) 1.5 g benzoic acid and 1.6 terephthalic acid. The benzoic acid melted at 121°; the content of COOH was determined by titration and found to be 36.59 (calculated 36.88%). The terephthalic acid melted at about 310° in a sealed tube; neutralization with KOH gave a COOH content of 53.17 and 55.44 compared with the calculated amount of 54.2%.

All these data permit us to represent the catalytic transformation by the following equation:

$$2C_6H_5CH_2CH_2C_6H_5 = C_6H_6 + C_6H_5CH_2CH_2C_6H_4CH_2CH_2C_6H_5$$

The transformation scheme in no way differs from the usual scheme for thermocatalytic transformation of alkylbenzenes.

In addition to the above-described reaction products, the higher fractions contained a more complex hydrocarbon, evidently formed with four phenyl groups linked by $-CH_2CH_2-$ groups.

TABLE 2
Ratio of Amounts of Toluene and Dimethylbenzene in Dependence on the Weight of Catalyst

Ditolylethane (g)	Catalyst (g)	Toluene (g)	Dimethylbenzene (g)	Ratio of toluene yield to dimethylbenzene yield
100	200	15.8	7.7	2.2
100	100	14.7	7.4	2.3
100	50	12.5	6.6	2.1

Ditolylethane. Three experiments were run with ditolylethane in the same conditions as with diphenylethane. In the third experiment were used 200 g catalyst (activated gumbrin) and 100 g ditolylethane. Fractionation of the products of transformation gave: 107-112°, 1.96 g; 112-134°, 2.1 g; 134-142°, 5.2 g; 142-160°, 1.9 g; 160-170°, 4.6 g; 170-330°, 21.0 g; above 330°, 35.9 g; losses 9.7 g.

The 107-112° fraction is mainly toluene, d_4^{20} 0.863. The 112-134° fraction is a mixture of toluene and xylene and was subsequently found to consist of equal parts of these hydrocarbons; similarly the 142-160° fraction was resolved into xylene and trimethylbenzene. The 134-142° fraction was xylene with d_4^{20} 0.862. Judging by the structure of the original ditolylethane, the latter fraction would be a mixture of m- and p-xylenes.

For the toluene type of transformation according to the equation

$$2CH_3C_6H_4CH_2CH_2C_6H_4CH_3 = C_6H_5CH_3 + CH_3C_6H_4CH_2CH_2C_6H_5CH_2CH_2C_6H_4CH_3$$

$$CH_3$$

the yield of toluene must amount to 47.1% of the theoretical yield. By analogy, for the xylene transformation the yield of xylene must be 25.2%. In practice the ratio of toluene to xylene is much higher; instead of 1.87:1 it is 4:1; hence it follows that the toluene decomposition must be regarded as the main reaction.

With progressive transformation of the ditolylethane heated with catalyst to a maximum temperature of 350°, the yield of distillate was 65% (calculated on the charge of raw material) in experiments with distillation of the reaction products. The ratio of the toluene to dimethylbenzene formed was substantially constant (Table 2).

In experiments with decomposition under a reflux condenser, when the formed reaction products were able to react for a long period with the catalyst, the ratio of toluene to dimethylbenzene was as high as 4:1. From this we can conclude that the dimethylbenzene formed itself participates in the further transformations with formation of methyl- and trimethylbenzene, as we had previously shown [2].

SUMMARY

1. Transformation of diphenylmethane in presence of aluminosilicate catalyst leads to formation of benzene alone in the volatile fraction.

2. Transformation of ditolylethane leads to initial formation of toluene and dimethylbenzene at the same time; increasing duration of contact with the catalyst increases the proportion of toluene due to secondary changes of the dimethylbenzene.

3. Formation of benzene from diphenylethane has an equilibrium character which is governed by the temperature.

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*See Consultants Bureau Translation, page 1535.

CONDENSATION OF ALLYLACETATE WITH BENZENE IN PRESENCE OF $AlCl_3$

I. P. Tsukervanik and S. G. Melkanovitskaya

Many authors have studied the condensations of allyl halides and allyl alcohol with benzene in presence of acid catalysts. Formation of 1,2-diphenylpropane has been observed in the majority of cases. In some cases, however, it was possible to isolate products containing one phenyl group. Nenitzesku [1] obtained 2-chloropropylbenzene together with 1,2-diphenylpropane from allyl chloride and benzene in presence of $FeCl_3$ and $ZnCl_2$. In our laboratory [2] allylbenzene and 2-chloropropylbenzene were obtained with the same catalyst and allyl alcohol. Allylbenzene was also obtained in low yields when using BF_3 [3], HF [4] and $AlCl_3$ [5]. In a recent paper Losev and co-workers [6] showed that condensations of allyl chloride in presence of $AlCl_3$ proceed in the first place with reaction of the chlorine atom, and the formed allylbenzene is subjected to various transformations. Consequently the literature data indicate that in the reactions discussed the double bond of allyl compounds only plays a part after substitution of the halogen or hydroxyl:

$$CH_2=CHCH_2-A + H-C_6H_5 \rightarrow C_6H_5CH_2CH=CH_2 \xrightarrow{HCl} C_6H_5CH_2CHCl-CH_3$$

$$C_6H_5CH_2-\underset{\displaystyle C_6H_5}{\underset{|}{CH}}-CH_3$$

where A = Cl, Br, OH.

Some condensations of allyl bromide and allyl chloride with benzene in presence of H_2SO_4 and HF have been described, however, which proceed only at the double bond [7].

We must also bear in mind that in certain specific conditions the condensations may lead almost entirely to anomalous products. Long ago the case was described of preparation from allyl chloride and benzene of propylbenzene in high yield [8].

We have studied the reaction of allylacetate with benzene with the aim of ascertaining whether addition at the double bond is possible.

The condensations of vinylacetate with benzene described by Korshak and co-workers [9] lead to acetophenone, 1,1-diphenylethane and 9,10-dimethyldihydroanthracene. Under the influence of $AlCl_3$ the first step is evidently cleavage of the ester linkage of vinyl acetate. On the other hand in our laboratory [10] it was possible in mild conditions to realize the normal condensation of vinylbutyl ether with benzene. One patent [11] claims the preparation of various β-phenyl compounds by condensation of vinyl derivatives (including vinyl acetate) with aromatic hydrocarbons in presence of $AlCl_3$.

It was to be expected that the great distance of the double bond from the ester group in allylacetate would cause the latter to react, if only partly, according to the following scheme:

$$CH_2=CHCH_2OCOCH_3 + H-C_6H_5 \rightarrow CH_3-\underset{\displaystyle C_6H_5}{\underset{|}{CH}}-CH_2OCOCH_3 \xrightarrow{+C_6H_5} CH_3-\underset{\displaystyle C_6H_5}{\underset{|}{CH}}-CH_2-C_6H_5$$

We started our study of the reactions by using small quantities of $AlCl_3$, but it was found that condensations do not then take place either in the cold or with heating. Only when using a slight excess of $AlCl_3$ over the equimolar amount (1.1 mole) can these condensations be effected. Evidently one mole $AlCl_3$ is bound to allylacetate in the form of a complex at the ester group. Subsequently, this complex reacts with benzene at the double bond, but the ether group then undergoes cleavage. In these experiments we obtained 1,2-diphenylpropane in yields of up to 56% of the theoretical. We were also able, by lowering the condensation temperature to 4-6°, to obtain small amounts of β-phenylpropyl acetate which was identified in the form of the corresponding alcohol. In one experiment it was shown that with an excess of benzene, β-phenylpropyl acetate gives 1,2-diphenylpropane. In none of our experiments was allylbenzene obtained.

All these facts justify us in believing that allylacetate actually reacts in the first instance at its double bond. We did not succeed in establishing the conditions in which β-phenylpropyl acetate would be the main product of the condensations. This is due to the ease of cleavage of the ester bond by the excess of $AlCl_3$.

In this group of condensations we thought it was very important to have a strict proof of the structure of the prepared diphenylpropane since the formation of two of its isomers is probable. No proof of this was submitted in previous papers; the authors limited themselves to determination of the constants and to some indirect criteria.

On nitrating 1,2-diphenylpropane, Konovalov [12] obtained a crystalline primary nitro compound which we used for identification of our product, although the reaction proceeds slowly and gives low yields.

By performing the synthesis according to the scheme:

$$C_6H_5CH_2MgCl + C_6H_5COCH_3 \rightarrow C_6H_5CH_2C(CH_3)(OH)C_6H_5 \rightarrow C_6H_5CH{=}CC_6H_5 \rightarrow C_6H_5CH_2CH(CH_3)C_6H_5$$

it was possible for us to nitrate two specimens of 1,2-diphenylpropane and to convince ourselves of their identity by the absence of depression of the melting point of a mixture of the two nitro compounds.

EXPERIMENTAL

Examples of condensation of allylacetate with benzene. 1) To 80 ml benzene, mixed with 16.1 g (0.12 mole) $AlCl_3$ was gradually added 10 g (0.1 mole) allylacetate in 20 ml benzene. The mixture was cooled with ice and stirred for 2 hours. After decomposition with acidified water, the benzene layer was separated, dried and fractionated to give 11 g (56%) 1,2-diphenylpropane with b.p. 128-130° at 8 mm; resinous residue 2.5 g.

2) To a solution of 10 g allylacetate in 100 ml benzene at room temperature was gradually added 16.1 g $AlCl_3$. The mixture was heated for $2^1/_2$ hours on a boiling water bath. Yield 11 g (56%) 1,2-diphenylpropane and 3 g resin.

3. To a solution of 15 g (0.15 mole) allylacetate in 150 ml benzene was added 24.2 g (0.18 mole) $AlCl_3$ small portions over a period of $2^1/_2$ hours with continuous cooling and stirring. Stirring was prolonged for another 2 hours. The temperature of the reaction mixture (thermometer in flask) was maintained throughout the whole period at 4-6°. A fraction was collected with b.p. 114-128° at 15 mm (3.4 g); judging by the saponification number, the fraction contained 54% β-phenylpropyl acetate; yield 7% of the theoretical. In addition 11.3 g (38%) 1,2-diphenylpropane was isolated.

Investigation of the products of condensations. β-Phenylpropyl alcohol was isolated by saponification of the 114-128° (15 mm) fraction. Liquid with a pleasant odor. B.p. 113-114° (16 mm).

d_4^{20} 1.0062; n_D^{20} 1.5275; MR_D 41.54; Calculated 41.81.

The p-nitrobenzoate was prepared with m.p. 61-62°. The constants are very close to those reported in the literature [13].

Dehydrogenation of β-phenylpropyl alcohol over copper catalyst at 250-300° and 20-40 mm residual pressure gave hydratropic aldehyde which was isolated via the bisulfite compound. It was identified as the semicarbazone, m.p. 152-153° [14].

1,2-Diphenylpropane. After two distillations the product of the condensations had the following constants: b.p. 128-130° (7 mm); d_4^{20} 0.9818; n_D^{20} 1.5581; MR_D 64.45; Calculated 64.43.

Control synthesis of 1,2-diphenylpropane. Benzylmethylphenyl carbinol [15] was prepared from 40 g benzyl chloride, 7.7 g magnesium and 32 g acetophenone. Yield 37 g (66%). Dehydration of the carbinol over Al_2O_3 at 400° gave methylstilbene in a yield of 46% of the theoretical. The best results were obtained by boiling the carbinol (22 g) with acetic anhydride (40 g) and acetyl chloride (20 g) [16]. The methylstilbene isolated after neutralization of the solution with soda was recrystallized from alcohol. M.p. 79-80°. Yield 16 g (79.5%).

Methylstilbene (9 g) was reduced to 1,2-diphenylpropane [17] with sodium (9 g) in alcoholic solution (100 ml) by heating the mixture on the boiling water bath. Complete solution of the sodium was effected by addition of 20 ml alcohol, after which the mixture was acidified. The 1,2-diphenylpropane was extracted with ether. Yield 7.7 g (85%).

After distillation over sodium the synthesized product had the following constants: b.p. 128-129° for 7 mm; d_4^{20} 0.9797; n_D^{20} 1.5581; MR_D 64.60.

Nitration of 1,2-diphenylpropane. 5 g diphenylpropane was heated at 100° in a flask, fitted with a mechanical stirrer and a reflux condenser, with 20 ml nitric acid (d 1.075). Heating was continued for 18-20 hours and was stopped after the whole of the hydrocarbon had been transformed into a heavy oil which collected at the bottom of the flask. After separation and washing with soda, the oil was treated with an aqueous alcoholic solution of KOH; only a small portion of the oil went into the alkali solution; from the latter, by passage of CO_2, was gradually separated the nitro compound which crystallized. After washing [illegible] aqueous alcohol and recrystallizing from alcohol, the substance had m.p. 153° as reported by Konovalov [12]. Both specimens of 1,2-diphenylpropane gave the same nitro compound, and a mixed sample melted without depression at 153°.

SUMMARY

1. The condensation of allylacetate with benzene in presence of $AlCl_3$ was studied in various conditions. In all cases the main product is 1,2-diphenylpropane (yield up to 56% of the theoretical).

2. At low temperatures (4-6°) the formation was demonstrated of the intermediate β-phenylpropyl acetate, which indicates that the first stage in the condensation is addition at the double bond.

3. Synthesis by a scheme excluding the formation of isomers gave 1,2-diphenylpropane whose nitration by the Konovalov method gave a primary nitro compound which enabled identification of the product of the described condensation.

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*See Consultants Bureau Translation, page 737.

**See Consultants Bureau Translation, page 329.

THE REACTION OF ETHER-OXIDES WITH NITROGEN COMPOUNDS

VII. REACTION OF GLYCIDE ISOPROPYL AND n-BUTYL ETHERS WITH DIETHYLAMINE

F. G. Ponomarev and V. G. Polosukhina

In previous communications by one of us [1-3] we described the results of experiments on addition of ammonia and diethylamine to methyl and ethyl ethers of glycide. Continuing our investigations, in this paper we describe the results obtained for the interaction of the isopropyl and n-butyl ethers of glycide with diethylamine, data for which are absent from the literature.

The experiments showed that these glycide ethers, like the methyl and ethyl ethers, easily react with aqueous diethylamine, forming the corresponding ethers of aminopropanediol (I) in high yield

$$(C_2H_5)_2NCH_2CHOHCH_2OR \qquad (I)$$

where R = iso-C_3H_7, C_4H_9.

This reaction proceeds in one direction and is not accompanied by side reactions, in contrast to the behavior of glycide which polymerizes when diethylamine is added to it during heating [4]; the glycide ethers react smoothly with this amine, independently of the order of mixing of the reactants, at room temperature and at a higher temperature (80-100°).

The structure of the prepared aminoalcohols follows from the method of preparation, in complete accord with the Krasusky rule [5] on the order of addition of ammonia and amines to unsymmetrical α-oxides and their substituted derivatives and is confirmed by their synthesis from diethylamine and the corresponding ethers of glycerol α-monochlorohydrin

$$ROCH_2CHOHCH_2Cl \xrightarrow{(C_2H_5)_2N} ROCH_2CHOHCH_2N(C_2H_5)_2$$

where R = iso-C_3H_7 and C_4H_9.

Esterification of the aminoglycols (I) with acetic anhydride gave the corresponding α,β-diesters of aminopropanediol (II)

$$(C_2H_5)_2NCH_2CH(OCOCH_3)CH_2OR \qquad (II)$$

The ethers of aminopropanediol (I) are colorless liquids with basic properties, less hygroscopic than the methyl and ethyl ethers of aminopropanediol [2,3]. They react with metallic sodium, rapidly decolorize bromine in chloroform and give crystalline picrates. They do not give crystalline hydrochlorides. When dry hydrogen chloride is passed into absolute ethereal solutions of the aminoalcohols, a viscous noncrystalline mass comes down. Neither do the bases (I) give crystalline derivatives with ethyl iodide.

EXPERIMENTAL

The glycide ethers required for the reaction were obtained from the corresponding ethers of glycerol α-monochlorohydrin under the action of pulverized KOH in absolute ether as already described [6]. Diethylamine was used in all the experiments in the form of 33% aqueous solution.

Reaction of glycide isopropyl ether with diethylamine. Synthesis of 3-isopropoxypropanol-2-diethylamine (I, R = iso-C_3H_7).

a) To 17.5 g (0.15 mole) glycide isopropyl ether (b.p. 134°, n_D^{20} 1.4111) was added 33 g (0.45 mole) diethylamine in 58 ml water. The temperature of the mixture was observed to rise from 20 to 30°. When the initially homogeneous reaction mixture was heated on the water bath, it separated into two layers after 10-15 minutes. After heating for 3 hours, the upper layer, which consisted of the aminoalcohol (I), was separated; saturation of the aqueous layer with KOH gave a further small quantity of aminoalcohol which was combined with the main product before drying over KOH and distilling in vacuum. There was obtained 23 g (80%) 3-isopropoxypropanol-2-diethylamine. Here and in all subsequent experiments the yield is calculated on the glycide ether. In two

other experiments conducted in precisely the same conditions, the product was obtained in yields of 75 and 77% of the theoretical.

b) To 11.6 g (0.1 mole) glycide isopropyl ether was added 21.9 g diethylamine (0.3 mole) in 44 ml water. The reaction mixture was stood at room temperature for 72 hours. Separation and purification in the above-described manner gave 13.8 g (73%) 3-isopropoxypropanol-2-diethylamine. In another experiment in which the amount of diethylamine was reduced from 3 to 2 moles per mole ether, the yield of product was slightly reduced (64% of the theoretical).

3-isopropoxypropanol-2-diethylamine had the following constants:

b.p. 93-95° at 10 mm; d_4^{20} 0.9856; n_D^{20} 1.4348; MR_D 55.06; found 55.48.

0.1562 g sub.: 8.3 ml 0.1N H_2SO_4. 0.1276 g sub.: 7.00 ml 0.1N H_2SO_4 (Kjeldahl). 0.1154 g sub.: 6 ml 0.1N NaOH. 0.1242 g sub.: 6.7 ml 0.1N NaOH. 0.2456 g sub.: 21.04 g benzene: Δt 0.34°. Found %: N 7.44, 7.46; OH 8.84, 9.17; M 195.8. $C_{10}H_{23}O_2N$. Calculated %: N 7.40; OH 8.98; M 189.29.

Here and in the later experiments the content of hydroxyl group was determined with the aid of acetic anhydride in pyridine [7].

It is a colorless liquid with the odor of imines. It possesses basic properties. It dissolves readily in alcohol, ether, carbon terachloride and benzene, sparingly in cold water and still more sparingly in hot water. It does not distil without decomposition at atmospheric pressure. It is stable when kept for a long period. It reacts with metallic sodium. It rapidly decolorizes a chloroform solution of bromine and potassium permanganate. In normal conditions it absorbs moisture. A quantity of 0.7259 g increased in weight by about 1% after 6 hours.

The picrate, prepared by mixing equimolar alcoholic solutions of the aminoalcohol and picric acid, forms lemon-yellow crystals with m.p. 163-164° (from absolute alcohol).

0.0892 g substance: 8.92 ml 0.1 N H_2SO_4 (Eckert's method [8]). Found %: N 14.00 $C_{16}H_{26}O_9N_4$. Calculated %: N 13.39

The acetate (II. R = iso-C_3H_7) was prepared by the action of acetic anhydride (20% excess) on aminopropanediol. Colorless liquid with a characteristic odor:

B.p. 88° at 8 mm; d_4^{20} 0.9363; n_D^{20} 1.4328; MR_D 64.23; Calculated 64.85.

0.1342 g substance: 5.3 ml 0.1 N H_2SO_4. 0.1210 g substance: 4.9 ml 0.1 N H_2SO_4 (Kjeldahl). Found %: N 5.53; 5.67. $C_{12}H_{25}O_3N$. Calculated %: N 6.05

The acetate is soluble in alcohol and ether; sparingly in water.

Action of diethylamine on the isopropyl ether of glycerol α-monochlorohydrin. With the objective of confirming the structure of the 3-isopropoxypropanol-2-diethylamine prepared from glycide isopropyl ether and diethylamine, we synthesized the same aminoalcohol from the corresponding ether of the haloalcohol and diethylamine. 3 g glycerol α-monochlorohydrin isopropyl ether (b.p. 180-184°, n_D^{20} 1.4405) prepared from epichlorohydrin and absolute alcohol [6], was sealed into a tube with 4.3 g (threefold excess) diethylamine; the mixture was heated on a boiling water bath for 4 hours. The product was then worked up with water; the upper layer was separated; the aqueous layer was saturated with solid KOH to give a small amount of upper layer which was combined with the main product before drying with KOH and distilling in vacuum. Yield 2.7 g (72.6%) aminoalcohol with b.p. 96-98° at 10 mm.

The picrate of this base melted at 163-164° (from absolute alcohol) and did not give a depression with the above-described picrate of the base prepared from glycide isopropyl ether and diethylamine.

0.1264 g substance: 12.41 ml 0.1 N H_2SO_4 (Eckert's method). Found %: N 13.75. $C_{16}H_{26}O_9N_4$. Calculated %: N 13.39.

Reaction of glycide butyl ether with diethylamine. Synthesis of 3-butoxypropanol-2-diethylamine (I. R = C_4H_9)

a) To 23 g (approx. 0.18 mole) glycide butyl ether (b.p. 164-166°; n_D^{20} 1.4178) was added 36.5 g (0.5 mole) diethylamine in 75 ml water. The temperature rose from 20 to 26° and the homogeneous liquid formed two layers after 10-15 minutes. Further procedure was as described above. Vacuum fractionation gave 27 g (76.7%) of 3-butoxypropanol-2-diethylamine. In two other similar experiments this aminoalcohol was obtained in yields of 74 and 77% of the theoretical.

b) To 13 g (0.1 mole) glycide ether was added 22 g (0.3 mole) diethylamine in 44 ml water and the mixture allowed to stand for 72 hours at room temperature. The product was worked up as before to give 13 g (64%) 3-butoxypropanol-2-diethylamine. Using 2 instead of 3 moles of diethylamine per mole glycide ether, the yield fell to 53%.

3-Butoxypropanol-2 diethylamine is a colorless liquid with an imine-like odor.

B.p. 118-119° at 12 mm; d_4^{20} 0.8864; n_D^{20} 1.4340; MR_D 59.71; Calculated 60.11.

0.2304 g substance: 10.9 ml 0.1 N H_2SO_4 (Kjeldahl). 0.1502 g substance: 7.2 ml 0.1 N H_2SO_4. 0.1308 g substance: 6.3 ml 0.1 N NAOH. 0.1164 g substance: 6.1 ml 0.1 N NaOH. 0.1206 g substance: 22.21 g benzene: Δt 0.17°. 0.2330 g substance: 22.21 g benzene: Δt 0.21°. Found %: N 6.62, 6.71; OH 8.21, 8.91: M (mean value) 208.8. $C_{11}H_{25}O_2N$. Calculated %: N 6.89; OH 8.37; M 203.32

It possesses basic properties; dissolves easily in alcohol, ether and benzene; sparingly in cold water and still more sparingly in hot. It is stable after prolonged storage. Distils at atmospheric pressure (180–185°) with much decomposition. Reacts with metallic sodium. Rapidly decolorizes potassium permanganate and bromine in chloroform. In ordinary conditions it takes up moisture. After 6 hours 0.4227 g took up 0.6%.

The picrate forms lemon-yellow crystals with m.p. 166-167° (from absolute alcohol).

0.0642 g substance: 6.3 ml 0.1 N H_2SO_4 (Eckert's method). Found %: N 13.74. $C_{17}H_{28}O_9N_4$. Calculated %: N 12.95.

The acetate (II. R = C_4H_9), prepared as described above, is a colorless oil with a characteristic odor.

B.p. 112-113° at 6 mm; d_4^{20} 0.9377; n_D^{20} 1.4344; MR_D 67.99; Calculated 69.47.

0.1306 g substance: 5.2 ml 0.1 N H_2SO_4. 0.1432 g substance: 5.9 ml 0.1 N H_2SO_4 (Kjeldahl). Found %: N 5.57, 5.77. $C_{13}H_{27}O_3N$. Calculated %: N 5.71.

The acetate is soluble in alcohol and ether, sparingly in water.

Action of diethylamine on glycerol α-monochlorohydrin n-butyl ether. A mixture of 4 g glycerol α-monochlorohydrin n-butyl ether (b.p. 203-205°, n_D^{20} 1.4428) and 5.3 g diethylamine (threefold excess) was heated in a sealed tube on a boiling water bath for 6 hours. The product was then treated with water (9 ml); the top layer was collected, dried with solid KOH and distilled in vacuum. Yield 3.7 g (74.9%) 3-butoxypropanol-2-diethylamine with b.p. 120-121° at 13 mm.

The picrate of this base melted at 166-167° (from absolute alcohol) and did not give a depression with the above-described picrate of the base obtained from glycide butyl ether and diethylamine.

0.1183 g substance: 10.54 ml 0.1 N H_2SO_4. Found %: N 12.44. $C_{17}H_{28}O_9N_4$. Calculated %: N 12.95.

SUMMARY

1. The reaction of glycide isopropyl and n-butyl ethers with aqueous diethylamine was studied.

2. The products of these reactions: 3-isopropoxypropanol-2-diethylamine and 3-butoxypropanol-2-diethylamine and their acetates and some salts were characterized.

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• See Consultants Bureau Translation, page 681.
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••• See Consultants Bureau Translation, page 985.

REACTIONS OF ALIPHATIC DIAZO COMPOUNDS WITH UNSATURATED COMPOUNDS

XVII. REACTION OF ETHYLDIAZOACETATE WITH ESTERS OF UNSATURATED ACIDS AND WITH MESITYL OXIDE IN PRESENCE OF COPPER CATALYSTS

I. A. Dyakonov, I. N. Somin and M. I. Komendantov

In previous communications one of us [1] put forward the suggestion that realization of the reaction between ethyldiazoacetate and olefins in presence of copper catalysts

$$R-CH=CH-R_1 + N_2CHCOOC_2H_5 \xrightarrow[\text{or } CuSO_4)]{Cu} \begin{matrix} CHCOOC_2H_5 \\ / \quad \backslash \\ RCH-CH-R_1 \end{matrix} + N_2 \qquad (1)$$

may meet with difficulty when the nucleophilic properties of the ethylenic components in this reaction are weakened by the presence of electron acceptor groups R and R_1 at the double bond. Up to now only one example illustrating this possibility [2] had been known: diethyl fumarate and the diazoacetate do not react with one another with formation of a cyclopropane derivative if the experiment is conducted in presence of copper powder; due to the decomposition of the ethyl diazoacetate on the copper catalyst, only a fresh quantity of ethyl fumarate is obtained [3].

In the present investigation we attempted to increase the number of these examples by studying the heterogeneous catalytic reaction of ethyl diazoacetate with esters of α,β-unsaturated acids – transcrotonic and methacrylic acids – as well as with an α,β-unsaturated ketone – mesityl oxide. It must be pointed out that no data have hitherto appeared in the literature concerning the reaction of carbonyl-containing compounds with aliphatic diazo compounds in presence of copper catalysts. In the absence of catalysts, α,β-unsaturated ketones react with aliphatic diazo compounds in the same manner as do esters of α,β-unsaturated acids [4], i.e., with formation of the corresponding pyrazolines. An example is the reaction of CH_2N_2 with mesityl oxide [5] and of $N_2CHCOOC_2H_5$ with benzalacetophenone [6]. Ketones not containing multiple bonds react with diazomethane usually in the presence of hydroxyl-containing catalysts. Products of the reaction are most usually α-oxides or homologs of the original ketones [7], but in isolated cases the formation occurs of cyclic ketoacetals due to interaction of 2 moles ketones with 1 mole CH_2N_2 [8]. Benzaldehyde reacts similarly with ethyl diazoacetate, in a molar ratio of 2 : 1, in the absence of copper catalyst [9].

In the present communication it is shown that ethyl diazoacetate does not enter into reaction with the ethyl ester of trans-crotonic acid (in presence of copper sulfate) according to equation (1): ($R = CH_3$, $R_1 = COOC_2H_5$). An experiment led to separation of ethyl fumarate – the product of dimerization of $2>CHCOOC_2H_5$ residues – in a yield of 53% of the theoretical. The ester of crotonic acid was recovered to the extent of 60% of the amount calculated from equation (1). In addition a considerable amount of resinous material was obtained.

Reaction did not take place with methylmethacrylate due to fairly rapid polymerization. Taking into account the inhibiting action of copper powder, we may assume that polymerization was accelerated by formation of radicals due to breakdown of the ethyl diazoacetate.

Investigation of the reaction with mesityl oxide showed that the product was an extremely complex mixture of esters, mostly high-boiling, whose separation involved great difficulties. The composition of this complex mixture appears to vary slightly in dependence on the rate of addition of ethyl diazoacetate in the condensation reaction. The slower the addition the closer the elementary composition of the main portion of product to the formula of the ester

$C_{16}H_{26}O_4$. Formation of the latter may be represented by the equation

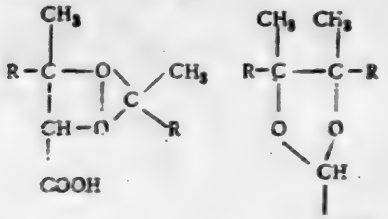
$$N_2CHCOOC_2H_5 + 2(CH_3)_2C{=}CH{-}COCH_3 \xrightarrow[(Cu)]{CuSO_4} C_{16}H_{26}O_4 + N_2. \qquad (2)$$

In experiment 1, in which the slowest addition (27 g/hr) was made, fractions 7 and 8 were closest to the composition $C_{16}H_{26}O_4$ (see table) and represented 50.6% by weight of all the fractions. From the lower-boiling portion were isolated fractions 4-6 (6.5% of the total weight), corresponding to the composition $C_{10}H_{16}O_3$:

$$N_2CHCOOC_2H_5 + (CH_3)_2C{=}CHCOCH_3 \xrightarrow[(Cu)]{CuSO_4} C_{10}H_{16}O_3 + N_2 \qquad (3)$$

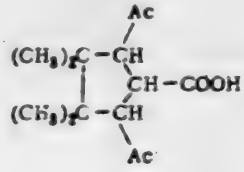
and fractions 1-2 (5-6% of the total weight), the main component of which was ethyl glycolate. The remaining fractions enumerated in the table were not examined.

Alkaline hydrolysis of fractions 7-8 gave a small amount of glycolic acid, a mixture of oily acids of indeterminate composition and a solid acid with m.p. 110° with the formula $C_{14}H_{22}O_4$, corresponding to the ester $C_{16}H_{26}O_4$. No explanation has yet been found for the formation of glycolic acid on hydrolysis: its ester could not have come over with the ester $C_{16}H_{26}O_4$ due to the too large difference in boiling points of these compounds. The liquid acids (equivalent 197) were not further investigated. On the basis of the literature data [8, 9] on the formation of cyclic condensation products in reactions of diazo compounds with aldehydes or ketones, we should expect structures (I) or (II) for the acid $C_{14}H_{22}O_4$



(I)

(II)



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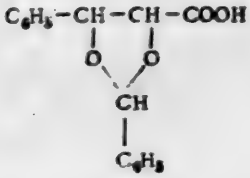
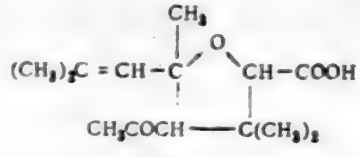


(IV)

where R = $(CH_3)_2C{=}CH-$ and Ac = $-COCH_3$.

The benzalphenylglyceric acid (IV), obtained by condensation of ethyl diazoacetate with benzaldehyde, hydrolyzes quantitatively to benzaldehyde and phenylglyceric acid [9] on heating with aqueous alcohol or with dilute acetic acid. In these conditions the acid $C_{14}H_{22}O_4$ does not hydrolyze. Under the action of acetic acid, however, it partly changes, possibly into an isomeric acid. Acid $C_{14}H_{22}O_4$ definitely isomerizes in presence of sulfuric acid: on heating together, a small amount of acetone is formed together with an acid of the same composition with m.p. 168° whose structure was not established. None of the anticipated products of hydrolysis were found. The data obtained were not consistent with formulas (I) and (II). Formula (III) could not be taken into consideration in view of the conspicuous unsaturation of acid $C_{14}H_{22}O_4$ (see below). We decided on the structure of the tetrahydrofuran carboxylic acid (V)*, although we failed in the course of further investigation to obtain conclusive evidence in support of this conclusion.



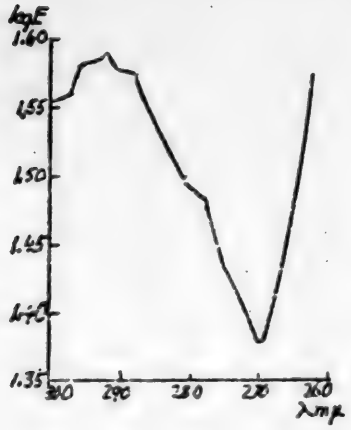
(V)

Starting from this formula, we may assume that 2% H_2SO_4 causes ring expansion with participation of the carbonyl of the acetyl group: the product of isomerization does not give a precipitate with 2,4-dinitrophenylhydrazine in contrast to the original acid. Acetone is evidently formed due to a side reaction of hydration of the isobutenyl

* Here we give only one of the four possible (for the given reaction) formulas of trimethyl-isobutenylacetyl-tetrahydrofuran carboxylic acid.

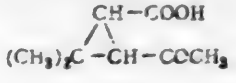
group similar to that observed for mesityl oxide in the same conditions [10].

The acid with m.p. 110° does not hydrogenate over Raney Ni in alcoholic solution at the ordinary temperature. In the same conditions it slowly adds on hydrogen in presence of platinum. The consumption of hydrogen exceeds that calculated for one double bond (40% excess). If formula (V) is correct, then the excess must be due to hydrogenolysis of the ether bond of the ring: in the hydrogenation product the active hydrogen content was higher than that calculated for $C_{14}H_{26}O_4$. The reaction with 2,4-dinitrophenylhydrazine gave a positive result. Rupture of the ring of the investigated acid evidently also accounts for the increased permanganate consumption during oxidation over that calculated for one double bond (70% excess). In the products of this reaction were found acetone and a little acetic acid (possibly due to further oxidation of the acetone), but instead of the expected dibasic acid $C_{11}H_{16}O_8$ more drastic oxidation gave a mixture of non-crystallizing acids whose analysis did not give definite results. Evidently the screening action of substituents on the ring hinders the formation of derivatives at the carbonyl group of the acid. A precipitate is only formed with 2,4-dinitrophenylhydrazine. The presence of a carbonyl group was conclusively demonstrated only by the ultraviolet spectrum of the acid. The acid has a maximum of absorption at $\lambda = 292$ mμ, i.e., in the region of adsorption of the C = O group. Fractions 4-5 were a mixture of isomeric esters $C_{18}H_{26}O_8$. Their alkaline hydrolysis gave (yield 15% of the theoretical) trans-3,3-dimethyl-2-acetylcyclopropane-1-carboxylic acid (VI), and formation of acetone was detected.



Absorption curve of acid $C_{14}H_{22}O_4$. Solvent 95% alcohol. Concentration: 0.02 mole/liter. Beckmann SF-11 spectrophotometer.

Oxidation of acid (VI) with sodium hypobromite gave trans-caronic acid (VII). Formation of acetone on hydrolysis and some qualitative reactions of the investigated fractions make probable the presence of the isomeric esters (VIII) and (IX) in the mixture. The presence of small amounts of water in the condensation product readily brings about hydrolysis of (IX) with formation of mesityl oxide and the ester of glycolic acid, which, as already mentioned, was found in Fractions 1-2. Judging by the analytical data for Fractions 4-5 (about 2% active hydrogen found) the presence in the mixture of a hydroxyl-containing ester (structure not established) can also be assumed. The presence of only trimethylene carboxylic ester can be said to be conclusively established in these fractions.



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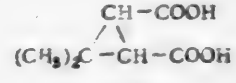
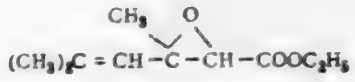
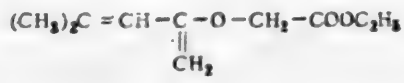


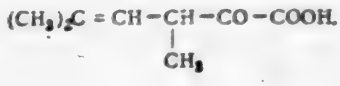
(VII)



(VIII)



(IX)



(X)

If addition of ethyl diazoacetate to mesityl oxide is effected more slowly than in experiment I (see experiment III), the main portion of the condensation product (54.9% of the weight of all the fractions) rather sharply deviates in composition from that calculated for $C_{16}H_{26}O_4$. Alkaline hydrolysis of this portion gives, apart from the acids obtained on hydrolysis of fractions 7-8 of experiment I, an unsaturated keto acid of the composition $C_8H_{12}O_3$ for which formula (X) may be advanced. The ethyl ester of this acid must have the composition $C_{10}H_{16}O_3$, and possibly its presence in the condensation brought about the above-noted change of composition.

Although our investigation is not complete, we can nevertheless draw a conclusion of interest to us concerning the behavior of the double bond in this reaction. It may be concluded, taking into account the insignificant yield of cyclopropane ether, that not the double carbon-carbon bond but the nucleophilic oxygen atom of mesityl oxide is the point of attack of the reagent – the $>CHCOOC_2H_5$ radical – in this reaction. In all probability, one of the esters – (VIII) or (IX) – is the primary product of interaction, while ester $C_{16}H_{26}O_4$ is formed by secondary reaction of mesityl oxide with one of these compounds.

However that may be, mesityl oxide or the esters of α,β-unsaturated acids concerned here cannot serve as a starting point for the preparation of derivatives of cyclopropane in this reaction. This result, in our opinion, may

be explained by a certain similarity of the electronic characteristics of the double bonds in the starting olefins.

EXPERIMENTAL

1. Reaction of Ethyl Diazoacetate with Mesityl Oxide

Experiment 1. Starting Components. Ethyl diazoacetate was purified by steam distillation in vacuum [11]. Mesityl oxide was rectified in a column; b.p. 126-130° [12]. The catalyst was anhydrous copper sulfate.

Condensation. To mesityl oxide (1230 g) and 4 g copper sulfate, heated to boiling on an oil bath, was slowly added dropwise with mechanical stirring a mixture of 400 g ethyldiazoacetate and 360 g mesityl oxide. The mean rate of addition was 27 g ethyl diazoacetate per hour. Bath temperature 130-140°. After nitrogen had ceased to come off (at the end of the experiment 93.4% of the calculated amount had come off) the reaction product was cooled and filtered and the excess mesityl oxide distilled off in vacuum: b.p. 60-70° at 60-65 mm, yield 1230 g. The residue was an oily liquid which was vacuum-distilled. The distillate weighed 530 g and boiled at 61° at 7 mm to 145° at 0.5 mm. Only the small low-boiling portion of the distillate was further fractionated in a vacuum column at 7 mm to 1 mm. The main high-boiling portion was distilled in a vacuum of less than 1 mm from a Wurtz flask with a low and broad side tube. The fractions resulting from repeated fractionation are set forth in the table.

Results of Fractional Distillation in Vacuum of the Condensation Product

No. of fraction	b.p. (°C)	Index of refraction n_D^{20}	Weight (g)	Weight in relation to total weight of fraction (%)
1	47.5-61 at 5 mm	1.4205	5.5	5.4*
2	51-55 at 5 mm	1.4188	17.0	
3	55-92	From 1.4206 to 1.4430	4.3	1.0
4	60-63 at 1 mm	1.4482	22.0	6.5*
5	60-62 at 1 mm	1.4510	5.0	
6	68-105 at 0.5 mm	From 1.4555 to 1.4654	62.1	15.0
7	105-115 at 0.5 mm	1.4701	95.0	50.6*
8	105-115 at 0.5 mm	1.4711	115.0	
9	105-130 at 0.5 mm	From 1.4730 to 1.4780	50.7	12.2
10	130-145 at 0.5 mm (with decomposition)	From 1.4780 to 1.4838	38.4	9.3

Investigation of first and second fractions. Both fractions, especially the first, contain, together with the ester of glycolic acid, mesityl oxide (characteristic odor, decolorization of $KMnO_4$, 2,4-dinitrophenylhydrazine test); this contamination also resulted (for the second fraction) in the not fully satisfactory analytical data and constants: b.p. 51-55° at 5 mm; d_4^{20} 1.0921; n_D^{20} 1.4188 (literature data: b.p. 156° at 760 mm; d_4^{15} 1.087 [10]).

0.1598, 0.1979 g substance: 0.2754, 0.3435 g CO_2; 0.1130, 0.1343 g H_2O. 0.1074, 0.1197 g substance: 24.1, 26.7 ml CH_4 (14°, 773.9 mm). 0.1037, 0.2035 g substance: 11.31, 18.13 g benzene: Δt 0.40; 0.50°. Found %: C 47.02, 47.37; H 7.91, 7.59; OH 16.32, 16.43; M 117.6, 115.2. $C_5H_8O_3$. Calculated %: C 46.15; H 7.74 OH 16.34; M 104.1.

Fraction 1 was not analyzed. Hydrolysis of 13.3 g of the second fraction with 100 ml 2 N NaOH followed by ether extraction of the acidified solution in a perforator gave 2.25 g glycolic acid with m.p. 78-79° (pressed on a plate and recrystallized from ether). It was identified by the mixed melting point test and by a determination of the equivalent.

0.1666 g substance: 21.83 ml 0.1 N NaOH. Found: equiv. 76.31. $(CH_2O)COOH$. Calculated: equiv. 76.06.

Hydrolysis of fraction 1 by heating with 10% HCl followed by evaporation of the solution likewise led to formation of glycolic acid.

Examination of fractions 4 and 5. Both fractions decolorized 2% $KMnO_4$, gave the silver mirror reaction with ammoniacal Ag_2O, and in the cold deposited iodine from a solution of KI in acetic acid.

*Calculated for sum of weights of both fractions.

Fraction 4: b.p. 60-64° at 1 mm; d_4^{20} 1.002; n_4^{20} 1.4482

0.1274, 0.1616 g substance: 0.3065, 0.3851 g CO_2; 0.1019, 0.1277 g H_2O. 0.1459 g substance: 4.1 ml CH_4 (13.5°, 768.4 mm) 0.2214 g substance: 14.72 g benzene: Δt 0.44°. Found %: C 65.61, 65.04; H 8.74 8.84; OH 2.0; M 175. $C_{10}H_{16}(OH)$. Calculated %: C 65.19; H 8.76; OH 9.8; M 184.2

Fraction 5: b.p. 64-68° at 1 mm; d_4^{20} 1.004; n_D^{20} 1.4510.

0.1141 g substance: 0.2726 g CO_2; 0.0903 g H_2O. 0.1416 g substance: 12.86 g benzene: Δt 0.29°. 0.4184 g substance: 11.5 ml 0.2 N KOH (hydrolysis). 0.1875 g substance: 5.0 ml CH_4 (13.5°, 768.4 mm). Found %: C 65.18; H 8.85; $M_{cr.}$ 168.0; $M_{hyd.}$ 182.0; OH 1.9. $C_{10}H_{16}OH$. Calculated %: C 65.19; H 8.76; M 184.2; OH 9.8.

Trans-3,3-dimethyl-2-acetylcyclopropane-1-carboxylic acid (VI). 5.4 g (0.3 mole) fraction 4 was hydrolyzed by heating for an hour with 25 ml 10% NaOH. The solution was steam-distilled. When the first portion of the distillate was mixed with an acetic acid solution of 4-nitrophenylhydrazine, it gave a yellow precipitate with m.p. 141-143° (0.2 g); after crystallization from aqueous alcohol the m.p. was 145-146°; identity was confirmed by a mixed melting point test with acetone 4-nitrophenylhydrazone.

The alkaline solution was acidified and the resultant oily acid was extracted with ether. The crystals obtained after removing the ether and drying in vacuum were pressed on a porous plate and crystallized from a mixture of ether and ligroine. M.p. 108-110°. Yield of acid (VI) 0.66 g (14%). Heating of fraction 5 for 3 hours with 10% NaOH led to formation of 0.71 g acid (VI) (15% of the theoretical yield) and 0.6 g acetone 4-nitrophenylhydrazone. In both cases prolonged extraction of the acid solution gave an insignificant amount of oily material which was not amenable to examination.

Acid (VI) is soluble in alcohol and ether, sparingly in water. It does not decolorize in the cold a solution of $KMnO_4$. Its silver salt was prepared.

0.1116 g sub.: 0.2525 g CO_2; 0.0797 g H_2O. 0.1002 g sub.: 6.4 ml 0.1N NaOH. Found %: C 61.76; H 7.97; equiv. 156.3. $C_8H_{12}O_3$. Calculated %: C 61.52; H 7.75; equiv. 156.2. 0.1566, 0.1367 g sub.: 0.0640, 0.0560 g Ag. Found %: Ag 40.87, 40.96. $C_8H_{11}O_3Ag$. Calculated %: Ag 41.00.

Oxidation with hypobromite: trans-carboxylic acid (VII). A solution of 0.75 g acid (VII) in 2.4 ml 10% NaOH was run in the cold into a cold solution of sodium hypobromite (44 ml H_2O, 2.64 g NaOH and 3.5 g bromine); bromoform was evolved. After the lapse of 2 hours, the solution was saturated with SO_2 and made alkaline; the bromoform was then extracted with ether. The aqueous layer was acidified with sulfuric acid and saturated with ammonium sulfate; this brought down a solid carboxylic acid which was extracted with ether. After careful evaporation of the solvent in the cold, the acid (VII) was twice recrystallized from hot water. M.p. 211° in agreement with the literature [10]. Yield 0.60-0.64 g or 80-85% of the theoretical. The acid equivalent and the silver content of the prepared salt were determined.

0.1511 g sub.: 19.0 ml 0.1N NaOH. Found: equiv. 79.49. $C_3H_8(COOH)_2$. Calculated: equiv. 79.08. 0.1983, 0.1509 g sub.: 0.1136, 0.0864 g Ag. Found %: Ag 57.28, 57.37.. $C_5H_6O_4Ag_2$. Calculated %: Ag 58.01.

Examination of fractions 7 and 8. Fraction 7, b.p. 105-115° at 0.5 mm; n_D^{20} 1.4701.

0.1471 g sub.: 0.3628 g CO_2; 0.1220 g H_2O. 0.2497 g sub.: 21.39 g benzene: Δt 0.20°. Found %: C 67.32; H 9.28; M 268.9. $C_{16}H_{26}O_4$. Calculated %: C 68.05; H 9.28; M 282.4.

Fraction 8: b.p. 105-115° at 0.5 mm; n_D^{20} 1.4711.

0.1280 g sub.: 0.3174 g CO_2; 0.1035 g H_2O. 0.1692 g sub.: 18.99 g benzene: Δt 0.17°. Found %: C 67.69; H 9.05; M 299.0. $C_{16}H_{26}O_4$. Calculated %: C 68.05; H 9.28; M 282.4.

Alkaline hydrolysis of fraction 7. 80 g of the substance was hydrolyzed by heating with 350 ml 10% KOH. Dark-red solution. After concentration on the water bath it was acidified with 30% sulfuric acid which was introduced in 10 ml portions beneath a layer of ether which had been poured on to the surface of the cooled alkaline solution. The organic acid which separated as an oil after acidification went into the ether layer which was periodically poured off and replaced by fresh ether. From the ethereal extracts was obtained 59 g oily acid which was distilled in vacuum (0.5 mm) from a Wurtz flask with a broad side tube. The first fraction of distillate crystallized in the side tube. The distillation was stopped and the crystals pressed on porous plate. M.p. 76-79°. Yield of crude glycolic acid 2 g. M.p. (from ether) 79-80°.

20.00 mg sub: 23.14 mg CO_2; 9.60 mg H_2O. 0.1613 g sub.: 23.71 ml 0.1 N NaOH. Found %: C 31.57; H 5.37; equiv. 75.61. $(CH_2O)COOH$. Calculated %: C 31.59; H 5.34; equiv. 76.05.

Distillation was resumed and a distillate obtained in the form of a very viscous oil with b.p. 115-135° (0.5 mm). It was separated into four fractions, differing from one another by viscosity and color; the viscosity increases in the later fractions, which have the appearance of vaseline; the color deepens from yellow in the first fraction to red-brown in the last. The two top fractions slowly crystallized when rubbed with a rod. On seeding, the lower fractions also crystallized but to a lesser degree. After standing for 48-72 hours all the fractions were filtered under vacuum through a porous Schott filter and the obtained crystals, as well as the filtrates, were combined. The crystals were washed with absolute ether and pressed on porous plate. Yield of crude acid $C_{14}H_{22}O_4$ with m.p. 100-104° was 10 g (14%). Crystallization from a mixture of ether and ligroine gave 6 g nearly colorless crystals with m.p. 108°. The pure preparation melted at 109-110°.

The oily filtrate, separated from the solid acid $C_{14}H_{22}O_4$ was again distilled in vacuum to give a yellow distillate (fairly viscous) and a small quantity of glycolic acid. The equivalent of the distillate was determined:

1.0150 g sub.: 51.18 mg 0.1N NaOH. Found: equiv. 197.6.

The distillate was not further examined. Glycolic acid was also isolated by prolonged ethereal extraction in a perforator of the acidic aqueous solution remaining after separation of the investigated mixture of acids.

Alkaline hydrolysis of fraction 8 (97 g substance, 430 ml 10% KOH) also led to formation of glycolic acid and acid $C_{14}H_{22}O_4$. 14 g of the latter (16%) was obtained; m.p. 102-105°. Crystallization gave 9 g with m.p. 107-108°.

Examination of acid $C_{14}H_{22}O_4$. M.p. 109-110°. Readily soluble in alcohol, less soluble in ether, insoluble in water. Decolorizes cold $KMnO_4$ solution.

0.1180, 0.1305 g sub.: 0.2865, 0.3185 g CO_2; 0.0942, 0.1038 g H_2O. 0.2250, 0.1548 g sub.: 8.85, 6.98 ml 0.1N NaOH. 0.0948 g sub.: 9.10 ml CH_4 (15°, 754.4 mm). Found %: C 66.27, 66.58; H 8.93, 8.92; act. H 0.404; equiv. 254.4, 255.7. $C_{14}H_{22}O_4$. Calculated %: C 66.12; H 8.72; act. H 0.396; equiv. 254.3.

Hydrogenation. The acid does not undergo hydrogenation over Raney nickel in alcoholic solution at room temperature. Hydrogenation of 1 g acid in alcohol (50 ml) in presence of 0.2 g Pt at 16° and 765 mm lasted 11 hours at an initial hydrogen absorption velocity of 15 ml in 30 minutes and a total H_2 consumption of 130 ml (0°, 760 mm), which exceeds by 45% the amount of hydrogen calculated for one double bond. The product of hydrogenation is a noncrystallizing, colorless oil, fairly viscous. The number of active hydrogens was found to be higher than calculated for $C_{14}H_{26}O_4$.

0.1091 g sub.: 12.0 mg CH_4 (15°, 754 mm). Found: act. H 0.458. Calculated: act. H 0.393.

Reaction with reagents at the carbonyl group. The semicarbazone and p-nitrophenylhydrazone of the acid could not be prepared by the usual procedures. On interaction of 1 g of 2,4-dinitrophenylhydrazine in a solution of 25 ml alcohol, 7.5 ml water and 5 ml conc. sulfuric acid [14] with an alcoholic solution of 0.5 g of the acid, a precipitate of hydrazone was only obtained after several hours. M.p. 102-105°. After three crystallizations from alcohol the m.p. was constant at 180-181°. Owing to lack of material it was not analyzed. See diagram for ultraviolet absorption spectrum of the acid.

Action of aqueous alcohol. The original acid was recovered unchanged after 45 minutes boiling of a solution of the acid in 50% alcohol followed by removal of the solvent on the water bath.

Action of 20% acetic acid. 0.5 g acid in solution in 20% acetic acid (20 ml) was refluxed for an hour. Removal of the solvent left 0.4 g yellowish, viscous mass, acidic in character. Analysis of the silver salt showed that hydrolysis had not taken place since the silver content of the salt did not differ from that calculated for the salt of the original acid (or its isomer).

0.1659 g sub.: 0.0491 g Ag. Found %: Ag 29.59. $C_{14}H_{21}O_4Ag$. Calculated %: Ag 29.86.

Action of 2% sulfuric acid. 0.5 g acid and a solution of 2% H_2SO_4 with a small addition of alcohol (for dissolving the acid) were heated for 2 hours under a reflux condenser and the solution was then steam-distilled. A little acetone was detected in the distillate with the help of the p-nitrophenylhydrazine test. Ether extraction in a perforator of the remaining aqueous solution yielded resin containing crystals which were recrystallized from aqueous alcohol. M.p. 167-168°, colorless crystals. Yield 0.2 g or 40% of the weight of the original acid. A second experiment was performed with 3 g acid and acetone was detected in the form of the 2,4-dinitrophenylhydrazone; yield of acid with m.p. 167-168° 1.4 g or 46% of the original weight. The analytical data for the acid and its silver salt are consistent with the formula $C_{14}H_{22}O_4$.

10.13 mg sub.: 24.84 mg CO_2; 7.78 mg H_2O. 0.2058 g sub.: 8.05 ml 0.1N NaOH. Found %: C 66.79; H 8.58; equiv. 255.8. $C_{14}H_{22}O_4$. Calculated %: C 66.12; H 8.72; equiv. 254.3. 0.0907 g sub.: 0.0270 g Ag. Found %: Ag 29.77. $C_{14}H_{23}O_4Ag$. Calculated %: Ag 29.86.

The acid is readily soluble in alcohol but less soluble than the original acid in ether and insoluble in water. A solid 2,4-dinitrophenylhydrazone is not formed even after prolonged standing of the acid with the reagent.

Oxidation of the acid $C_{14}H_{22}O_4$ with m.p. 109-110°. 5 g of the acid was oxidized in alkaline solution with 2% $KMnO_4$ solution (in the cold). Consumption of oxidizing agent was 10.5 g (170% of that calculated for one double bond). After working up in the usual manner, acetone was isolated from the neutral reaction products (as the p-nitrophenylhydrazone), while ether extraction of the acid products gave a small amount of acetic acid and 3.6 g of a glutinous, noncrystallizing acid with a dark-red color. Both acids were converted into their silver salts and the neutralization equivalent of the second acid was determined.

0.2345 g sub.: 0.1510 g Ag. Found %: Ag 64.40. $C_2H_3O_2Ag$. Calculated %: Ag 64.63. 0.2239, 0.2336 g sub.: 0.2465, 0.2573 g CO_2; 0.0722, 0.0766 g H_2O; 0.0970, 0.1010 g Ag. Found %: C 30.04, 30.05; H 3.61, 3.67; Ag 43.35, 43.23. $C_{11}H_{16}O_2Ag_2$. Calculated %: C 28.84; H 3.08; Ag 47.11. 0.2770 g sub.: 18.82 ml 0.1N NaOH. Found: equiv. 147.2. $C_{11}H_{16}O_4$. Calculated: equiv. 122.1.

Judging by the analytical data, the noncrystallizing acid is not pure but a mixture of acids. Attempts to separate them by fractional precipitation of the silver salts were unsuccessful. The phenacyl ester was a liquid.

2. Reaction of Ethyl Diazoacetate with Mesityl Oxide in Experiments II and III

Experiments II and III were carried out by the same procedure as Experiment I, except for a change in the mean rate of addition of $N_2CHCOOC_2H_5$ to mesityl oxide (expt. II—35 g/hr.; expt. III—40 g/hr.) and a different molar ratio reagents (1:4 in experiments II and III against 1:4.6 in expt. I). Below are set forth the analytical data characterizing the principal fractions obtained on fractional distillation of the crude product of these experiments (compare the data for fractions 7 and 8 of expt. I, distilling in approximately the same temperature range).

Expt. II. Fraction with $n_D^{25.4}$ 1.4692-1.4730 (53% of the weight of all the fractions).

0.0992, 0.1529 g sub.: 0.2421, 0.3729 g CO_2; 0.0817, 0.1269 g H_2O. 0.1726, 0.1718 g sub.: 15.50, 15.65 g benzene: Δt 0.19, 0.19°. Found %: C 66.73, 66.56; H 9.22, 9.26; M 300.6, 286.3. $C_{15}H_{26}O_4$. Calculated %: C 68.06; H 9.28; M 282.3.

Expt. III. Fraction with n_D^{20} 1.466; d_4^{20} 1.040 (54.9% of weight of all fractions).

0.1204, 0.1267 g sub.: 0.2873, 0.3018 g CO_2; 0.0944, 0.0985 g H_2O. 0.3212, 0.3565 g sub.: 12.97, 14.21 g benzene: Δt 0.45, 0.47°. Found %: C 65.13, 65.00; H 8.77, 8.70; M 292.3, 273.8. $C_{15}H_{26}O_4$. Calculated %: C 68.06; H 9.28; M 282.3.

80 g of this fraction was subjected to hydrolysis with 10% KOH in the conditions described in expt. I. From the products of this reaction, apart from a mixture of oily acids, were isolated glycolic acid (0.7 g) and, in contrast to expt. I, a solid acid with m.p. 63° (from ether-ligroine) in a weight of 7.0 g. Repeated crystallizations from the same solvent gave m.p. 64-65°.

0.1267, 0.1083 g sub.: 0.2990, 0.2658 g CO_2; 0.0955, 0.0820 g H_2O. 0.1339 g sub.: 6.79 ml 0.1N NaOH. 0.1054 g sub.: 11.25ml CH_4 (11.5°, 759 mm). Found %: C 64.40, 64.71; H 8.43, 8.47; equiv. 197.2; OH 7.86. $C_{14}H_{22}O_4$. Calculated %: C 66.11; H 8.72; equiv. 254.3; OH 6.68. $C_8H_{12}O_3$. Calculated %: C 61.51; H 7.74; equiv. 156.2; OH 10.88.

The data suggest the formation of a mixture of acids which cannot be separated by crystallization from ether. Fractionation was found possible by treatment of the mixture (6.7 g) with a large amount of hot water: the water-insoluble portion (2.5 g) had m.p. 106-108° (from aqueous alcohol) and was identified by the mixed test with acid $C_{14}H_{22}O_4$ (m.p. 109-110°). From the solution was isolated (by ether extraction) another acid with m.p. 71-72°, 0.9 g; after crystallization from ether-ligroine the m.p. was 72-73°.

0.1262, 0.1249 g sub.: 0.2853, 0.2835 g CO_2; 0.0871, 0.0886 g H_2O. 0.1072 g sub.: 16 ml CH_4 (12.5°, 751.5 mm). 0.1167 g sub.: 7.44 ml 0.1N NaOH. Found %: C 61.79, 61.94; H 7.72, 7.94; OH 10.82, equiv. 156.8. $C_8H_{12}O_3$. Calculated %: C 61.51; H 7.74; OH 10.88, equiv. 156.2.

The acid is poorly soluble in cold water, easily in alcohol, less easily in ether; it decolorizes permanganate solution in the cold; with an acetic acid solution of p-nitrophenylhydrazine it gives a yellow solid with m.p. 135-137°.

In addition expt. III gave fractions with approximately the same constants as in expt. I: b.p. 68-75° at 2 mm, $n_D^{25.2}$ 1.4490-1.4530. They comprised 10% of the whole weight. The middle one of these fractions with b.p. 71.5-73° at 2 mm; $n_D^{25.2}$ 1.4520 (6.5% of the weight of the whole distillate) was analyzed.

0.1141 g sub.: 0.2726 g CO_2; 0.0903 g H_2O. 0.2547 g sub.; 13.07 g benzene: Δt 0.603°. 0.4184 g sub.: 11.5 ml 0.2 N KOH (hydrolysis). Found %: C 65.18; H 8.85; $M_{cr.}$ 165.8; $M_{hyd.}$ 182.0. $C_{10}H_{16}O_3$. Calculated %: C 65.19; H 8.76; M 184.2.

Qualitative reactions were the same as for fractions 4 and 5 in expt. I. A fraction corresponding to glycolic ester was not isolated.

3. Reaction of Ethyl Diazoacetate with the Ethyl Ester of Trans-Crotonic Acid

0.5 g copper sulfate, 80 g (0.07 mole) ethyl crotonate with b.p. 136-138° and 40 g (0.35 mole) pure ethyl diazoacetate were reacted as described previously. At the end of the reaction 63.6 g crotonic ester (5.57 moles) was regenerated as compared with the calculated amount (0.35 mole); b.p. 35-37° at 14 mm. The residual reaction product (39 g) was distilled in a 10 mm vacuum: b.p. 95-105°, $n_D^{14.1}$ 1.4410. Yield of crude fumaric ester: 16.2 g (53%). Literature data [13]: b.p. 218.4°; n_D^{20} 1.4410; d_4^{15} 1.057. About 20 g of undistillable resins were obtained. After redistillation in vacuum the ester was characterized by its constants and by analysis:

d_4^{20} 1.055; n_D^{20} 1.440.

0.1505 g sub.: 0.3069 g CO_2; 0.1005 g H_2O. Found %: C 55.54; H 7.46. $C_9H_{16}O_4$. Calculated %: C 55.68; H 7.03. $C_{10}H_{16}O_4$. Calculated %: C 63.10; H 8.47.

In addition diphenacyl fumarate was obtained with m.p. 196-197° (from alcohol), and was identified by comparison with an authentic sample.

4. Reaction of Ethyl Diazoacetate with Methyl Methacrylate

Dropwise addition was made slowly with stirring to 120 g methyl methacrylate (b.p. 100-101°) at the boil (with 0.5 g copper powder) of a solution of 31 g ethyl diazoacetate in a volume equal to that of the methacrylate. Nitrogen was given off. After an hour polymerization had proceeded to a degree such that the reaction product did not flow out of the flask.

A blank experiment (without ethyl diazoacetate) run in the same conditions showed much less polymerization after one hour.

SUMMARY

1. Interaction of ethyl diazoacetate with esters of trans-crotonic and methacrylic acid in presence of copper or copper sulfate does not lead to formation of the corresponding esters of cyclopropane carboxylic acids. In the former case the product of reaction is fumaric ester; in the second case rapid polymerization sets in before the completion of the experiment.

2. Interaction of ethyl diazoacetate with mesityl oxide in presence of copper catalysts proceeds in various directions and leads to formation of an extremely complex mixture of esters. The main direction of this interaction when there is a large excess of mesityl oxide in the reaction is condensation of two molecules of mesityl oxide with one molecule of ethyl diazoacetate. Secondary reactions are condensation of reactants in 1:1 molar ratio and formation of ethyl glycolate.

3. The ester of 3,3-dimethyl-2-acetylcyclopropane carboxylic acid was found only to an insignificant extent among the various substances formed in this condensation and investigated in this communication.

4. The results obtained in this communication have been shown to fit in with previously formulated [1, 2] theoretical considerations about the laws regulating the interaction of ethyl diazoacetate with olefins in presence of copper catalysts.

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BORON FLUORIDE AS A CATALYST IN ORGANIC CHEMISTRY

IX. ALKYLATION OF o- AND p-CHLOROPHENOLS WITH 2-PENTENE IN PRESENCE OF BORON FLUORIDE ETHERATE

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Alkyl phenols and alkyl phenol ethers are widely used at the present time as antioxidants, as starting materials for synthesis of high-quality oil-soluble resins, pharmaceuticals, etc.. Alkyl halophenols and alkyl ethers of halophenols possess germicidal and insecticidal properties and are therefore of definite interest.

The simplest, most convenient and most accessible method of their preparation is the alkylation of phenols and halophenols with olefins in presence of various catalysts.

We have studied the alkylation of o- and p-chlorophenols with 2-pentene, obtained as a by-product in the production of synthetic rubber by the Lebedev process, in presence of boron fluoride etherate as catalyst.

Alkylation was studied at a temperature of 16-18° on a boiling water bath using various ratios of reactants in presence of 5-7% of catalyst.

It was established that o- and p-chlorophenols are alkylated by 2-pentene in presence of boron fluoride etherate with formation of a mixture of ethereal and phenolic products. The quantitative ratio between the ethereal and phenolic compounds depends on the temperature, the duration of reaction and the ratios of the main components. As a rule, rise of temperature from room to 100° promotes speedier reaction. For instance, on interaction of o-chlorophenol with 2-pentene in molar ratios, nearly identical yields of ethereal compounds (36%) are obtained at room temperature in the course of 5 days and at 100° in the course of 4 hours. At 100° the duration of reaction has the effect that up to 4 hours the yield of ethereal compounds rises, while subsequently, up to 16 hours it decreases slightly. At the same time the yield of phenolic compounds increases. These observations once again confirm the correctness of the hypothesis that alkylation of phenols with olefins at higher temperatures proceeds through formation of alkyl ethers and isomerization of these to alkyl phenols. However, this hypothesis does not exclude the possibility also of direct alkylation of the benzene ring of phenolic ethers, especially at relatively low temperatures.

EXPERIMENTAL

Starting materials. The chlorophenols needed for reaction were used in the form of ordinary commercial preparations. o-Chlorophenol, freshly distilled with b.p. 171-173° and d_{20}^{20} 1.2480. p-Chlorophenol without previous recrystallization. 2-Pentene was isolated from the still residues of production of synthetic rubber by the S. V. Lebedev process [1].

Alkylation procedure. Chlorophenols and $BF_3 \cdot O(C_2H_5)_2$ were introduced into a small flask. The mixture was cooled with snow and 2-pentene was added. The homogeneous, readily mobile, light-brown liquid was left at room temperature for a definite period in the closed flask or heated on the boiling water bath. It was then treated with 5% aqueous NaOH until the phenolic product had completely separated, i.e. until a drop of the alkali-insoluble mass gave a turbidity with dilute hydrochloric acid. Thereupon the ethereal compounds (in the form of a pleasant-smelling oily liquid) were separated from the aqueous-alkaline solution of phenolic compounds, washed with water, dried with ignited sodium sulfate or potassium carbonate and distilled. Fractions were collected over a wide temperature interval. A small quantity of viscous, black resin, readily soluble in ether, always remained in the distillation flask.

The alkaline solutions of phenolic products were treated with dilute hydrochloric acid until neutral. The regenerated phenols were separated, washed with water, dried and distilled (like the ethereal compounds) over a wide temperature interval.

The experimental data for the reaction with o-chlorophenol are set forth in Table 1, and those for p-chlorophenol in Table 2.

TABLE 1

Alkylation of o-Chlorophenol with 2-Pentene in Presence of $BF_3 \cdot O(C_2H_5)_2$

No. of expt.	Taken for reaction				Molar ratios of phenol to 2-pentene	Conditions of reaction		Products obtained					
								Ethereal type			Phenolic type		
	o-Chlorophenol (in g)	2-Pentene (in g)	$BF_3 \cdot O(C_2H_5)_2$ (in g)	(in %)		Temp.	Duration (in hrs)	in g	in %•	b.p.	in g	in %•	b.p.
1	12.73	6.44	1.06	6.2	1:1	Room	5 days	6.26	34.30	50-125° (10 mm)	1.42	7.78	180-250°
2	10.36	5.70	1.25	7.8	1:1	95-97°	2	4.54	28.32	210-296	3.71	23.14	200-267
3	13.27	6.55	0.95	4.8	1:1	95-97	4	6.53	35.18	125-240 (10 mm)	2.33	12.55	180-255
4	12.18	7.70	1.24	6.2	1:1	95-97	16	5.48	27.56	120-210 (10 mm)	4.13	20.77	180-260
5	6.43	6.40	1.10	8.6	1:2	95-97	4	5.33	41.54	120-168 (13 mm)	3.20	24.94	180-260
6	13.70	3.65	1.25	7.2	2:1	95-97	4	2.95	28.53		6.15	59.48	180-260

We see from Table 1 that o-chlorophenol is alkylated by 2-pentene in presence of 6% $BF_3 \cdot O(C_2H_5)_2$ at room temperature with formation of almost exclusively ethereal products (expt. 1). Heating of reactants in 1:1 ratios on the boiling water bath for up to 4 hours raises the yield of ethereal products and lowers the relative yield of phenolic compounds (expts. 2 and 3). More prolonged heating is accompanied by the usual phenomenon characteristic of this type of reaction: the yield of ethereal compounds falls and that of phenolics rises, since side by side with alkylation reactions we now get the reaction of isomerization of the alkyl phenolic ethers to alkyl phenols; the latter process is more significant the more easily the alkyl phenolic ethers isomerize.

Similar observations are made in the reaction with p-chlorophenol as shown in Table 2.

TABLE 2

Alkylation of p-Chlorophenol with 2-Pentene in Presence of $BF_3 \cdot O(C_2H_5)_2$

No. of expt.	Taken for reaction				Molar ratios of Chlorophenol to 2-pentene	Conditions of reactions		Products obtained					
								Ethereal type			Phenolic type		
	p-Chlorophenol (in g)	2-Pentene (in g)	$BF_3 \cdot O(C_2H_5)_2$ (in g)	(in %)		Temp.	Duration (in hrs)	in g	in %••	b.p.	in g	in %••	b.p.
1	12.45	7.60	1.35	6.8	1:1	95-97°	4	7.50	37.04	125-165° (9 mm)	2.30	11.36	121-140° (9 mm)
2	12.10	6.40	1.30	7.0	1:1	95-97	8	5.80	31.35		4.15	22.43	
3	12.30	3.90	1.45	8.9	2:1	95-97	4	5.25	47.51		—	—	

Interaction of o-chlorophenol with 2-pentene in 1:2 ratio for 4 hours at the temperature of the boiling water bath raises the yield of both the ethereal and the phenolic products (expt. 5, Table 1) in comparison with the reaction of components in 1:1 ratio. In these conditions o-chlorophenol almost completely enters into reaction and the total yield of products of alkylation is 66%. With a 2:1 ratio of chlorophenols to 2-pentene (expt. 6, Table 1; expt. 3, Table 2) the 2-pentene reacts quantitatively but the phenols are recovered to a considerable extent. At the same time in the reaction with o-chlorophenol the yield of ethereal products is much lower than in the same conditions in the reaction with p-chlorophenol.

Identification of products of alkylation. Sec.-amyl ethers of o- and p-chlorophenols, also sec.-amyl-substituted o- and p-phenols have not been described in the literature. For this reason the widely boiling fractions of ethereal and phenolic products were mixed and again fractionated into narrower fractions.

• In exps. 1, 3, and 6 the yield was calculated on the 2-pentene; in all other experiments on the total sum of components.

•• Yield calculated on total sum of components in expt. 1 and on 2-pentene in experiments 2 and 3.

In this way the following compounds were isolated.

1. Sec-amyl-o-chlorophenol. Colorless mobile liquid with a faint odor of o-chlorophenol; b.p. 137-140° at 11 mm.

d_4^{21} 1.0821; n_D^{21} 1.5250; MR_D 56.24; calculated 55.79.

10.61 mg sub.: 25.77 mg CO_2; 7.13 mg H_2O. 9.98 mg sub.: 24.12 mg CO_2; 6.95 mg H_2O. 0.1918 g sub.: 0.1384 g AgCl. Found %: C 66.28, 65.96; H 7.52, 7.73; Cl 17.85. $C_{11}H_{15}OCl$. Calculated %: C 66.47; H 7.61; Cl 17.86.

2. Sec-amyl ether of sec-amyl-o-chlorophenol. Colorless liquid with a pleasant odor; b.p. 121-124° at 10 mm.

d_4^{21} 0.9914; n_D^{21} 1.5010; MR_D 79.81; calculated 79.00.

11.77 mg sub.: 30.95 mg CO_2; 9.50 mg H_2O. 8.49 mg sub.: 22.32 mg CO_2; 6.99 mg H_2O. 0.1392 g sub.: 0.0757 g AgCl. Found %: C 71.78, 71.74; H 9.02, 9.23; Cl 13.45. $C_{16}H_{25}OCl$. Calculated %: C 71.46; H 9.38; Cl 13.20.

3. Sec-amyl ether of disec-amyl-o-chlorophenol. Colorless liquid with a pleasant odor; b.p. 140-144° at 10 mm.

d_4^{21} 0.9854; n_D^{21} 1.5052; MR_D 102.00; calculated 102.09.

11.32 mg sub.: 30.54 mg CO_2; 9.68 mg H_2O. 9.19 mg sub.: 24.81 mg CO_2; 7.93 mg H_2O. 25.952 mg sub.: 0.392 ml 0.02 N $AgNO_3$. 29.127 mg sub.: 0.442 ml 0.02 N $AgNO_3$. Found %: C 73.62, 73.68; H 9.59, 9.66; Cl 10.72, 10.78. $C_{21}H_{35}OCl$. Calculated %: C 74.39; H 10.42; Cl 10.47.

4. Sec-amyl-p-chlorophenol. Colorless mobile liquid. Crystallized overnight m.p. 51°, b.p. 130-131° at 8 mm; n_D^{20} 1.5308.

3.795 mg sub.: 9.340 mg CO_2; 2.950 mg H_2O. 6.400 mg sub.: 15.825 mg CO_2; 4.880 mg H_2O. 0.1659 g sub.: 0.1220 g AgCl. Found %: C 67.17, 67.30; H 8.69, 8.53; Cl 18.19. $C_{11}H_{15}OCl$. Calculated %: C 66.47; H 7.61; Cl 17.86.

5. Sec-amyl ether of o-sec-amyl-p-chlorophenol. Liquid with pleasant odor; b.p. 147-152° at 10 mm.

d_4^{20} 0.9895; n_D^{20} 1.4970; MR_D 79.47; calculated 79.00.

4.555 mg sub.: 12.085 mg CO_2; 3.775 mg H_2O. 5.125 mg substance: 13.565 mg CO_2; 4.230 mg H_2O. 0.1509 g substance: 0.0794 g AgCl. Found %: C 72.40, 72.23; H 9.27, 9.23; Cl 12.55. $C_{16}H_{25}OCl$. Calculated %: C 71.46; H 9.38; Cl 13.20.

In addition to the compounds described, the reaction with o-chlorophenol also gave a product with b.p. 165-166° at 10 mm (d_4^{21} 0.9334; n_D^{21} 1.5012), whose chlorine content was 5.1% (Carius). It was a fairly viscous, yellow liquid with a pleasant odor. Its composition was not established.

Consequently, with the help of boron fluoride etherate in the above-described conditions it is possible to introduce two alkyl groups into the benzene ring, already containing one substituent atom in the o- or p-position. It is a striking fact that the phenolic products isolated included only one sec-amyl-o-chlorophenol and one sec-amyl-p-chlorophenol. The sec-amyl ethers of chlorophenols were not isolated in sufficient quantity for identification.

SUMMARY

A study was made of the alkylation of o- and p-chlorophenols with 2-pentene, a by-product of the production of synthetic rubber by the Lebedev process, in presence of boron fluoride etherate.

The following were prepared and characterized: sec-amyl-o-chlorophenol; sec-amyl ether of sec-amyl-o-chlorophenol; sec-amyl ether of disec-amyl-o-chlorophenol; sec-amyl-p-chlorophenol; and sec-amyl ether of o-sec-amyl-p-chlorophenol.

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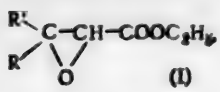
Laboratory of Organic Chemistry of the Voronezh State University

COMPOUNDS CONTAINING A THREE-MEMBERED OXIDE RING

VII. REACTION OF β, β-DIMETHYLGLYCIDAMIDE WITH CYCLOHEXYL-, DICYCLOHEXYL- AND BENZYLAMINES

V. F. Martynov

In previous communications devoted to the reaction of addition of aromatic amines to glycidic acids of the formula (I) where R and R' are aliphatic radicals, we established that in this case the rupture of the oxide ring of the glycidic acid takes place on the side of the tertiary carbon atom. The compounds resulting from this are α-hydroxy-β-arylamino-derivatives of the corresponding fatty acids. We arrived at this conclusion because these compounds lose carbon monoxide when treated with strong sulfuric acid, this being a well-known property of α-hydroxy acids. The second component of such a decomposition is bound to be the corresponding α-aminoaldehydes; however, we never obtained the latter, their place being taken in every case by the corresponding indole homologs. In the conditions of this reaction the α-aminoaldehydes which must have been formed would evidently undergo further transformations leading ultimately to an indole structure. A scheme for this transformation was submitted in the preceding communication [1]. In a certain sense, however, this scheme was hypothetical, in that we did not isolate a single one of the intermediate products that we proposed. Of course, we can here only speak of the separation of an aminoaldehyde, for the remaining intermediate compounds cannot be stable in presence of hot, strong sulfuric acid.

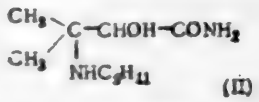


(I)

We resolved to demonstrate the validity of this scheme, i.e. to isolate the aminoaldehyde formed in this reaction. For this purpose it was necessary to exclude the possibility of secondary transformations of the aldehyde group. This could be done by replacing the aromatic amine by some aliphatic amine. As the latter we selected cyclohexylamine because it satisfied these requirements and, moreover, in size of molecule it was closest to aniline, which offered us the possibility of approaching most closely to the structure of the investigated compounds. Another advantage of this choice was that the aminoaldehyde which we might obtain in this case would inevitably be poorly soluble in water so that its isolation would be greatly facilitated.

Reaction of β,β-dimethylglycidamide with cyclohexylamine was effected by heating equimolecular amounts of these components in solution in absolute alcohol at 120-130°. The reaction gave a crystalline compound whose analysis identified it as the amide of hydroxycyclohexylamino-isovaleric acid.

By analogy with compounds that we had previously studied, the structure of this compound must be represented by formula (II). Treatment with strong sulfuric acid actually resulted in evolution of carbon monoxide which confirmed our proposed structure. However, this decomposition took place at a much higher temperature than we had observed for the corresponding compounds containing the residue of an aromatic amine. Whereas, for example, the ethyl ester of α-hydroxy-β-(p-toluidino)-isovaleric acid started to give off carbon monoxide at 110° [1], the compound here described only gave off carbon monoxide at 170-180°.

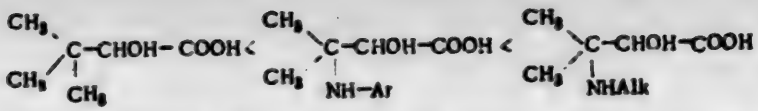


(II)

Rise of basicity of the amine leads to strengthening of the bond between the carboxyl and the α-carbon atoms. In this connection it is interesting to compare the decomposition of tert-butylglycolic acid with sulfuric acid. The structure of this compound is very similar to that of the hydroxyamino acids now under consideration, but differs in that in place of an amino group there is a methyl radical and the latter, as we know, has an electronic shift opposite to that of the ammonium ion*. We might, thus, expect tert-butylglycolic acid to be decomposed by sulfuric acid in milder conditions. Indeed, it does decompose when heated to only 50° [2].

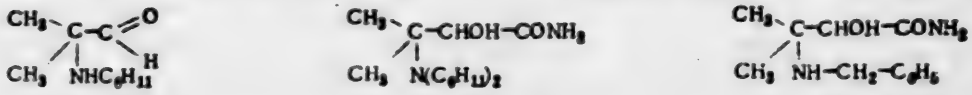
Consequently, the stability of α-hydroxy acids may be correlated with the inductive effect of the group in the β-position. The more pronounced the I-effect of these groups, the more stable will be the α-hydroxy acid. In respect of their stability, the compounds in question may be arranged in the following order:

*Here we must remember that the amino group does not function here in its free state, but in the form of the ammonium ion, since the reaction takes place in a medium of sulfuric acid.



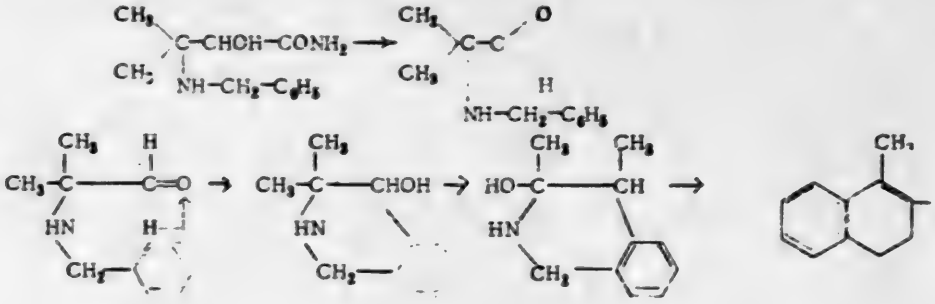
The second fragment of molecule obtained on decomposition by sulfuric acid of the amide of α-hydroxy-β-hexylamino-isovaleric acid was a liquid with a pronounced aliphatic amine odor. This compound gave a silver mirror and a crystalline derivative with 2,4-dinitrophenylhydrazone. The analytical data showed that we had indeed obtained α-cyclohexylamino-isobutyraldehyde (III). Thus our proposed scheme obtained one more proof of its validity.

Reaction of β,β-dimethylglycidamide with dicyclohexylamine was effected by a method similar to that already described. We obtained a crystalline compound to which, by analogy with the one described above, we attributed the formula of α-hydroxy-β-dicyclohexylamino-isovaleramide (IV). Under the action of strong sulfuric acid this compound likewise underwent decomposition, but the reaction proceeded at the very limit of decomposition of compounds with hydrochloric acid (above 180°) and therefore a very small amount of the corresponding aldehyde could be isolated and the only evidence we obtained of its aldehydic character was the silver mirror.



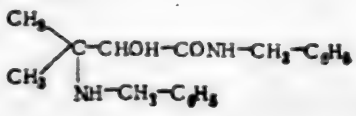
(III) (IV) (V)

The product of addition of benzylamine to β,β-dimethylglycidamide that we obtained under the action of strong sulfuric acid underwent decomposition at 170-180° with loss of carbon monoxide. This behavior coupled with the analytical data enabled us to ascribe to it the formula of α-hydroxy-β-benzylamino-isovaleramide (V). In this case, however, no compound could be isolated, apart from CO, by the action of concentrated sulfuric acid; when the solution was made alkaline, no emulsion of basic compound was formed, although here we might have expected the formation of a dimethylated dihydroisoquinoline



This might be explained either by complete decomposition of the formed substance (which is highly improbable since the corresponding aminoaldehyde had been isolated when α-hydroxy-β-hexylamino-isovaleramide was decomposed in the same conditions) or, what is more probable, by sulfonation of the dimethyldihydroisoquinoline which might have been formed. Sulfonation could easily have proceeded at the given temperature of decomposition, and sulfonic acids as a rule dissolve readily in water at any pH, thus accounting for our failure to isolate any compound after making the solution alkaline.

We then prepared the free acid from α-hydroxy-β-benzylamino-isovaleramide. The amino group was removed with barium hydroxide. Benzylamine was also reacted with the ethyl ester of β,β-dimethylglycidic acid and gave a compound to which, by analogy with those described above, was ascribed the formula of the benzylamide of α-hydroxy-β-benzylamino-isovaleric acid (VI).



(VI)

EXPERIMENTAL

Preparation of α-Hydroxy-β-cyclohexylamino-isovaleramide

5 g β,β-dimethylglycidamide and 4.3 g cyclohexylamine were dissolved in 30 ml absolute ethyl alcohol and sealed into an ampoule which was heated for 6 hours at 120°. Crystals separated on cooling and after crystallization from 30-40% alcohol melted at 164-165°. Yield 5 g (54%).

0.1028 g sub.: 12 ml N_2 (22°, 760.8 mm). 0.0990 g sub.: 11.4 ml N_2 (22°, 760.8 mm) Found %: N 13.15, 13.03. $C_{11}H_{22}O_2N_2$. Calculated %: N 13.08.

Preparation of α-Cyclohexylamino-isobutyralaldehyde

5 g α-hydroxy-β-cyclohexylamino-isovaleramide was placed in 20 ml strong sulfuric acid. The mixture was heated with frequent shaking over a bare flame (thermometer in liquid). At 160° gas bubbles (carbon monoxide) started to come off and the liquid darkened. At 180° copious gas evolution started and the odor of sulfur dioxide was pronounced. Heating was concluded without waiting for complete cessation of gas evolution. The hot, dark liquid was poured onto ice, the solution then being only weakly colored. On neutralizing with sodium carbonate and, toward the end, with KOH solution, an emulsion was formed which was distilled with steam. The compound was extracted from the water with ether. The ethereal extract was dried, the ether driven off and the residue distilled in vacuum. Yield 1.6 g (41%) of light-yellow liquid with b.p. 84-87° at 4 mm. The substance had a definite fatty amine odor and gave a silver mirror.

$n_D^{18.5}$ 1.4677; $d^{18.5}$ 0.9385; MR_D 50.02. $C_{10}H_{19}ON$. Calculated: MR_D 49.79.

With 2,4-dinitrophenylhydrazine a precipitate was obtained which contained a sulfuric acid residue linked like a salt with the amino group of the aldehyde. Due to this structure, the dinitrophenylhydrazone was fairly highly soluble in aqueous alcohol.

The sulfuric acid residue was removed by dissolving the 2,4-dinitrophenylhydrazone of the aminoaldehyde in aqueous alcohol and adding to the solution an aqueous solution of sodium acetate. A copious precipitate of hydrazone at once came down. M. p. 153-154°.

0.0631 g sub.: 11.2 ml N_2 (22°, 761.5 mm). 0.0790 g sub.: 14.1 ml N_2 (22°, 761.5 mm). Found %: N 20.25, 20.36. $C_{16}H_{22}O_4N_6$. Calculated %: N 20.06.

The aldehyde crystallized after standing for a few days; apparently a trimer was obtained; m.p. 114-115° after recrystallization from ligroine.

Preparation of α-Hydroxy-β-dicyclohexylamino-isovaleramide (with E. S. Varshavskaya)

9 g β,β-dimethylglycidamide was dissolved in 20 ml absolute ethyl alcohol and the solution mixed with 16 g dicyclohexylamine. The mixture was sealed into an ampoule and heated for 6 hours at 120°. A dark, viscous liquid was obtained which crystallized after a few days. Yield 10 g crude product or 45% of the theoretical. After repeated recrystallization from 30% aqueous alcohol the m.p. was 113.5-114°.

0.1037 g sub.: 8.3 ml N_2 (17°, 760.2 mm). 0.1054 g sub.: 8.5 ml N_2 (17°, 760.2 mm). Found %: N 9.68, 9.42. $C_{17}H_{32}O_2N_2$. Calculated %: N 9.6.

Decomposition of α-hydroxy-β-dicyclohexylamino-isovaleramide under the action of strong sulfuric acid. 2 g of the amide was placed in 10 ml strong sulfuric acid. The amide went into solution on heating. At 180° gas began to come off with a strong odor of sulfur dioxide. The solution darkened considerably. Without waiting for cessation of gas evolution, the mixture was poured onto ice. After neutralization, the dark solution was distilled with steam and in the distillate collected a few drops of substance with the distinct odor of an aliphatic amine and which gave a good silver mirror.

Interaction of β,β-Dimethylglycidamide with benzylamine (with Z. M. Gofung)

10 g of the amide in 30 ml absolute ethyl alcohol was heated with 9 g benzylamine in a sealed tube at 130° for 9 hours. Crystals of the amide of α-hydroxy-β-benzylamino-isovaleric acid separated on cooling. Yield 10 g (52%). After recrystallization from water the m.p. was 90-91°.

0.1062 g sub.: 12 ml N_2 (18°, 745 mm). 0.1005 g sub.: 11.3 ml N_2 (18°, 744 mm). 0.0216 g sub.: 0.1141 g camphor: Δt 36°. 0.0112 g sub.: 0.1637 g camphor: Δt 13°. Found %: N 12.82, 12.73; M 211.3, 210.7. $C_{12}H_{18}O_2N_2$. Calculated %: N 12.61; M 222.0.

Preparation of α-Hydroxy-β-benzylamino-isovaleric Acid

1.5 g amide of α-hydroxy-β-benzylamino-isovaleric acid was heated in a round bottomed flask under a reflux condenser with 2.6 g barium hydroxide in 25 ml water for 8 hours. The barium was precipitated with sulfuric acid removed with barium carbonate. The precipitate of barium sulfate was filtered off and the filtrate evaporated in vacuum to a small volume. A fine crystalline mass appeared after standing for 2 days in a vacuum desiccator and had m.p. 70-71° after recrystallization from water. Yield 0.25 g or 16.6% of the theoretical yield.

0.0935 g substance: 5.2 ml N_2 (22°, 764 mm). 0.0867 g substance: 4.8 ml N_2 (22°, 764 mm). Found %: N 6.37, 6.33. $C_{12}H_{17}O_3N$. Calculated %: N 6.27.

Interaction of Ethyl β,β-Dimethylglycidate with Benzylamine

10 g ethyl β,β-dimethylglycidate was heated in a sealed tube with 15 g benzylamine and 25 ml ethyl alcohol to 150-160° for 9 hours. After this period the ethyl alcohol was removed in vacuum, leaving in the flask a light-brown resinous mass which did not crystallize after standing for two days. A portion of this mass was treated with steam and then dried in a vacuum-desiccator. In this manner crystals of the benzylamide of α-hydroxy-β-benzylamino-isovaleric acid were formed and had m.p. 88-89° after three recrystallizations from ligroine.

0.0851 g substance: 6.9 ml N_2 (22°, 749 mm). 0.0697 g substance: 5.5 ml N_2 (22°, 766 mm). 0.0685 g substance: 15.16 g benzene: Δt 0.08°. 0.0850 g substance: 17.1 g benzene: Δt 0.09°. Found %: N 9.09, 9.05; M 290.4, 285.0. $C_{19}H_{24}O_2N_2$. Calculated %: N 8.97; M 312.0.

Hydrochloride of the Benzylamide of α-Hydroxy-β-Benzylamino-Isovaleric Acid

This was prepared from the second portion of resinous mass left in the flask (see above) by the action of concentrated hydrochloric acid. The salt was twice recrystallized from ethyl alcohol; m.p. 228°.

0.4400 g substance: 24.7 ml 0.1 N H_2SO_4. 0.4735 g substance: 25.4 ml 0.1 N H_2SO_4. Found %: N 7.72, 7.85. $C_{19}H_{25}O_2N_2Cl$. Calculated %: N 8.05.

SUMMARY

1. The reaction of β,β-dimethylglycidamide with cyclohexyl-α, dicyclohexyl-β and benzylamines was investigated. The following compounds which have not been described in the literature were obtained: α-Hydroxy-β-cyclohexylamino-isovaleramide; α-hydroxy-β-dicyclohexylamino-isovaleramide; α-hydroxy-β-benzylamino-isovaleramide; the benzylamide of α-hydroxy-β-benzylamino-isovaleric acid; α-hydroxy-β-benzylamino-isovaleric acid; α-cyclohexylamino-isobutyraldehyde.

2. The possibility of transition from glycidic acids to α-aminoaldehydes was exemplified by the preparation of α-cyclohexylamino-isobutyraldehyde from β,β-dimethylglycidamide.

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[2] G. Glückmann, Monatsch, 12, 356 (1891).

Received May 18, 1953

Zhdanov Leningrad State University
Chair of Theory of Structure

* See Consultants Bureau Translation, page 1047.

COMPOUNDS CONTAINING A THREE-MEMBERED OXIDE RING

VIII. REACTION OF ETHYL β,β-TETRAMETHYLENEGLYCIDATE WITH ANILINE

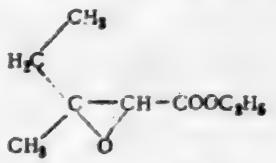
V. F. Martynov

We have investigated the addition of aromatic amines to glycidic acids with reference to the ethyl esters of β,β-dimethyl and β-methyl-β-ethylglycidic acids [1, 2].

Rupture of the oxide ring of these glycidic acids under the action of aromatic amines took place always at the same point, namely from the side of the tertiary carbon atom; however, the speed of addition of aromatic amines changes abruptly on passing from β,β-dimethyl- to β-methyl-β-ethylglycidic acid.

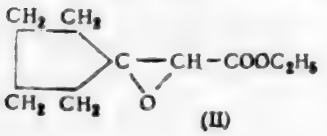
Whereas heating for 8 hours was sufficient for ethyl β,β-dimethylglycidate with aromatic amines of the type of aniline or p-toluidine in order to obtain a satisfactory yield [1], for ethyl-β-methyl-β-ethylglycidate (I) the same yield could only be obtained under otherwise identical conditions after heating for 40 hours [2].

This illustrated the great steric hindrance due to the introduction of another methyl group into the compound. Due to the free rotation along the axis of the carbon-carbon bond, the methyl group of the ethyl radical is suspended, as it were, over the oxide ring and thereby hinders the approach of reactants to the ring. In this connection it was interesting to investigate the addition of aromatic amines to those glycidic acids in which substituents in the β-position were linked to the ring and were thereby either deprived completely of the ability to change their position in space or only possessed very limited mobility. Special interest is attached in this respect to β,β-tetramethyleneglycidic acid (II) in which, due to the planar structure of the five-membered ring, substituents at the tertiary carbon atom are at the maximum distance from the oxide ring. It might therefore be expected that the addition of aromatic amines would proceed much more intensively than in the case of β,β-dimethyl- and β-methyl-β-ethylglycidic acids notwithstanding that in the latter the volume of substituents in the β-position is smaller than in β,β-tetramethyleneglycidic acid.



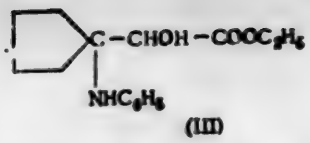
(I)

We carried out an investigation with ethyl β,β-tetramethyleneglycidate which we prepared by condensation of cyclopentanone with ethyl chloroacetate in toluene solution in presence of metallic sodium. This method requires less time and gives a higher yield than the condensation with sodium ethylate [3]. We performed the interaction with an aromatic amine (aniline) by the usual method of heating the glycidic ester with three times the amount of aniline in a sealed tube at 170-180°. It was found that in this case the addition of aniline takes place more energetically than with either of the two esters of glycidic acid mentioned above. Heating for 8 hours led to nearly quantitative yield of addition product. Thus, the above-mentioned considerations are actually relevant.



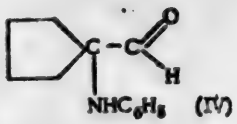
(II)

Concerning the point of rupture of the oxide ring of glycidic acid under the action of aniline, we established it by our previously applied method [1, 2]. Treatment of the addition product with concentrated sulfuric acid with heating resulted, even at 110°, in commencement of vigorous evolution of gas bubbles (carbon monoxide); no resinification whatever was observed, and the solution acquired faint yellow color. This behavior permitted us to claim with a high degree of probability that we were dealing with the ethyl ester of α-hydroxy-β-anilino-β,β-tetramethylenepropionic acid (III), since only α-hydroxy acids split off carbon monoxide under the action of sulfuric acid.

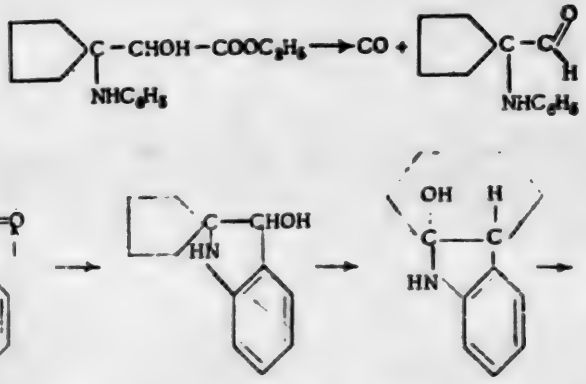


(III)

For conclusive proof it would have been necessary to isolate the second fragment of the molecule which must consist of anilino-tetramethyleneacetaldehyde (IV). As we showed in previous communications, however [1, 2], these arylamino aldehydes are unstable in a medium of concentrated sulfuric acid and undergo further transformations to give the corresponding indole homologs. In the present case the amino aldehyde (IV) should be converted into tetrahydrocarbazole whose formation may be represented by the scheme:



(IV)



We obtained a quantitative yield of a crystalline substance whose melting point was actually that of tetrahydrocarbazole. It gave a picrate melting at the same temperature as tetrahydrocarbazole picrate. For conclusive proof of its structure we synthesized tetrahydrocarbazole by E. Fischer's method [4]. Mixed melting tests of the two compounds as well as of their picrates did not give a depression. Consequently, we have definitely established both the structure of the product of addition of aniline to ethyl β,β-tetramethyleneglycidate and the mechanism of transformation of anilino-tetramethyleneacetaldehyde. A retropinacolin rearrangement had here taken place with ring expansion.

EXPERIMENTAL

Synthesis of Ethyl Tetramethyleneglycidate

This synthesis was not performed by the literature procedure [3]. A mixture of 73 g cyclopentanone and 120 g ethyl monochloroacetate was added with intensive stirring to 20 g finely powdered sodium in toluene. In order to initiate the reaction the addition of the mixture to the sodium was carried out at the ordinary temperature, but as soon as a temperature rise was observed the flask was immersed in ice and salt and the addition of the mixture of cyclopentanone and ethyl monochloroacetate was continued at such a rate that the temperature of the reaction mixture did not rise above +5°.

At the end of the reaction the contents of the flask had changed into a dark, gelatinous mass. On the following day, the reaction mass was decomposed with water, when the dark color disappeared.

The toluene extract was dried with sodium sulfate. The reaction product distilled at 113-114° at 13 mm. Yield 71 g (50%). The literature method gave 41% [3].

Reaction of Ethyl Tetramethyleneglycidate with Aniline

A mixture of 20 g ethyl tetramethyleneglycidate and 30 g aniline (three times the amount of aniline) was sealed into a glass ampoule and heated for 8 hours at 170-180°. At the conclusion of heating the ampoule was left overnight; the contents crystallized. The crystals were pressed and recrystallized 4 times from ligroine to give 20 g white, silky needles (65%). Allowing for the unavoidable losses during 4 crystallizations, we may estimate the yield at 80-90%. M.p. 117-118°.

0.1350 g substance: 6.5 ml N_2 (20°, 759.5 mm). 0.1685 g substance: 7.7 ml N_2 (20°, 756 mm). Found %: N 5.53, 5.23. $C_{15}H_{21}O_2N$. Calculated %: N 5.32.

Reaction of Ethyl α-Hydroxy-β-anilino-β,β-tetramethyleneglycidate with Strong Sulfuric Acid

To 5 g substance was added 40 ml concentrated sulfuric acid. On heating, the substances mutually dissolved. At 110-120° intensive evolution of carbon monoxide was observed and the mixture acquired a faint yellow color.

After gas bubbles had ceased to come off at the indicated temperature range, the reaction mixture was poured onto ice; white crystals of tetrahydrocarbazole came down and were drained and washed with water; quantitative yield. M.p. 113-114° after recrystallization from aqueous alcohol.

0.0976 g substance: 8.9 ml N_2 (18°, 759 mm). Found %: N 8.1. $C_{12}H_{13}N$. Calculated %: N 8.2.

Other authors give m.p. 110 to 120° [4, 5]. Authentic tetrahydrocarbazole which we synthesized by Fischer's method also melted at 113-114°.

The picrate obtained from both tetrahydrocarbazoles melted at 144-145°. In both cases the mixed melting test did not give a depression.

SUMMARY

1. The reaction between ethyl tetramethyleneglycidate and aniline was investigated. It was established that the oxide ring of this ester is ruptured at the side containing the tertiary β-carbon atom.

2. A new method of synthesis of tetrahydrocarbazole was developed.

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• See Consultants Bureau Translation, page 1637.

CONFIGURATION AND PROPERTIES

OF UNSATURATED ACIDS AND THEIR DERIVATIVES

THE REACTIVITY OF ESTERS OF OLEIC AND ELAIDIC ACIDS

E. G. Maleeva

In a study of the reactivity of oleic and elaidic acids [1] it was found that the differing reactivities of these stereoisomers is consistent with the theory of steric hindrance and confirms the theory that oleic and elaidic acids are respectively cis- and trans-isomers. It was also established that the methyl esters of oleic and elaidic acids are saponified (by alkali), hydrogenated and oxidized at different velocities. It was important to verify this observation for other derivatives of oleic and elaidic acids. It was also necessary to establish whether and to what extent the composition and structure of the alcohol radical influenced the reactions. Starting from these considerations, we have studied the reactivity of propyl oleate, isopropyl oleate, butyl oleate and benzyl oleate, also their geometrical isomers prepared from elaidic acid.

Experiments on saponification, hydrogenation and oxidation were carried out in the conditions previously described by us in work with methyl oleate and methyl elaidate; in this connection it transpired that saponification with alcoholic alkali of all the oleates, like that of methyl oleate, proceeds rather more slowly than in the case of the corresponding elaidates. On the other hand, oleates are hydrogenated and oxidized more quickly than elaidates.

Consequently, the experimental data indicate that the space round the ester groups of oleates is blocked to some extent by the hydrocarbon radical $CH_3(CH_2)_7$, which hinders access to it of the alkali elements. This is apparently not the case with elaidates, and their saponification therefore proceeds more quickly. From this standpoint the results of experiments on saponification confirm the cis-structure of oleates and the trans-structure of elaidates.

This conclusion becomes even more convincing when we consider the results of hydrogenation and oxidation of oleic and elaidic acids and their esters.

Concerning the role of the alcohol radical as a factor creating steric hindrance, we succeeded in observing relatively little difference between the reactivities of the benzyl esters. Here the benzyl group appears to retard saponification to a greater extent than any other alcoholic group in the esters that we studied.

Reactions at the double bond proceed rather more slowly with benzyl elaidate than in the other elaidates.

EXPERIMENTAL

1. Synthesis of esters of oleic and elaidic acids. Propyl oleate was prepared from silver oleate (1 mole) and propyl bromide (4 moles). A mixture of the salt and the bromide was first shaken for 3 hours and then heated for 30 minutes on a boiling water bath under a reflux condenser. At the conclusion of the reaction the mixture was diluted with dry ether, filtered and fractionally distilled. The ester was a light yellow liquid without odor; b.p. 220-220.5° (13 mm). d^{15} 0.8699.

Isopropyl oleate. Light-yellow with b.p. 218° (16 mm), d^{15} 0.8678 was prepared analogously to the above from silver salt and isopropyl bromide.

Butyl oleate was prepared in the form of a colorless liquid (similar to the above) by heating the components for 5 hours at 110° on an oil bath under a reflux condenser. B.p. 225-226° (15 mm), d^{15} 0.8670.

Benzyl oleate was synthesized from oleic acid (1 mole) and benzyl alcohol (3 moles) in presence of sulfuric acid. The mixture was heated for 8 hours on a boiling water bath; after washing with water, the product was dissolved in ether, neutralized with alcoholic KOH and carefully washed with water until free from alkali. Benzyl oleate distilled in vacuum at 235-239° (6-7 mm). A light-yellow oil, b.p. 216-218° (1 mm), d_4^{25} 0.9315, n_D^{25} 1.4820. At 23° it dissolves in 5 parts alcohol.

Propyl elaidate. From the Ag salt of elaidic acid and propyl bromide; b.p. 217° (12 mm), d^{25} 0.8710.

Isopropyl elaidate. From the Ag salt and isopropyl bromide, b.p. 218° (15 mm), d^{25} 0.3671.

Butyl elaidate. From the Ag salt and butyl bromide, b.p. 228° (14 mm), d^{18} 0.8671.

Benzyl elaidate was prepared in a similar manner to benzyl oleate. A light-yellow, oily liquid, b.p. 227-229° (1 mm), d^{25} 0.9372, n_D^{25} 1.4840. Less soluble than benzyl oleate in alcohol.

2. Saponification with alcoholic alkali. Saponification of each pair of isomeric esters was effected simultaneously in two identical vessels fitted with platinum electrodes and well ground covers. To each vessel, containing a weighed amount of ester equivalent to 0.0005 mole, was added 2 ml 0.1 N alcoholic KOH. Temperature, 28°. The start of each experiment was taken as the instant of addition of the alkali; immediately afterwards the first determination of electrical conductivity of the solution was carried out; after another 30 minutes a second determination of electrical conductivity was carried out; after 90 minutes a third and after 150 minutes a fourth determination was carried out. In other respects the experimental procedure was the same as described in our previous communication [2]. In Table 1 are set forth the results of observations of the rate of saponification of the esters from the change in electrical conductivity whose fall in the present case depends on the fall in concentration of the hydroxyl ions consumed in saponifying the ether.

TABLE 1

Compound	Change of electrical conductivity, time (in minutes)			
	0	30	90	150
Propyl oleate	571	534	514	515
Propyl elaidate	561	515	492	487
Isopropyl oleate	571	537	515	512
Isopropyl elaidate	564	548	495	487
Butyl oleate	571	534	520	520
Butyl elaidate	564	512	495	492
Benzyl oleate	571	540	525	528
Benzyl elaidate	563	512	500	487

3. Hydrogenation of esters of oleic and elaidic acids. Results of similar experiments have already been published but were carried out in other conditions [3]. The results here presented are also supplemented by data for hydrogenation of the benzyl esters.

The esters were hydrogenated in presence of platinum supported on $BaSO_4$; materials used in each experiment were 0.25 g $BaSO_4$ with 0.008 g Pt, 15 ml ethyl alcohol and 0.005 mole of the ester.

All experiments were performed at 28° in a hydrogenation apparatus, experiments with two isomeric esters being run side by side (Table 2).

TABLE 2

Compound	Amount of hydrogen added (in ml)		
	20 min.	40 min.	60 min.
Propyl oleate	45	80	103
Propyl elaidate	37	73	92
Isopropyl oleate	45	79	104
Isopropyl elaidate	38	73	90
Butyl oleate	44	80	104
Butyl elaidate	38	72	86
Benzyl oleate	40	65	100
Benzyl elaidate	32	72	80

TABLE 3

Compound	Change of electrical conductivity, duration (in minutes)			
	3	15	30	45
Propyl oleate	391	425	465	500
Propyl elaidate	400	417	434	465
Isopropyl oleate	391	434	465	500
Isopropyl elaidate	391	400	434	454
Butyl oleate	400	434	476	500
Butyl elaidate	400	417	434	466
Benzyl oleate	400	434	465	500
Benzyl elaidate	391	417	444	444

4. Oxidation of esters of oleic and elaidic acids. We had already established that methyl oleate and methyl elaidate do not react equally easily with aqueous $KMnO_4$. In this investigation, therefore, we also evaluated the oxidation of the esters by the change of electrical conductivity of aqueous $KMnO_4$ [1].

Oxidation experiments were carried out simultaneously with equal weights of isomeric esters (1/1500 mole). To the weighed amount of ester was added 5 ml 1.5% aqueous $KMnO_4$; the first measurement of electrical conductivity was made after 3 minutes, the second after 15, the third after 30 and the fourth after 45 minutes. Temperature 27°. The data are set forth in Table 3.

Thanks are due to Prof. A. K. Plisov for valuable advice during this investigation.

SUMMARY

1. Benzyl oleate and benzyl elaidate were synthesized and their properties described.

2. It was established that in harmony with the theory of steric hindrance the oleates are saponified more slowly than the elaidates and are oxidized and hydrogenated more quickly than elaidates.

3. The reactions of saponification, oxidation and reduction of oleic and elaidic acids and their esters confirm the structure of these acids as cis- and trans-isomers respectively.

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• See Consultants Bureau English translation, page 69

•• See Consultants Bureau English translation, page 71

SYNTHESIS OF 1,1-DIALKYLCYCLOPROPANES FROM ALDEHYDES

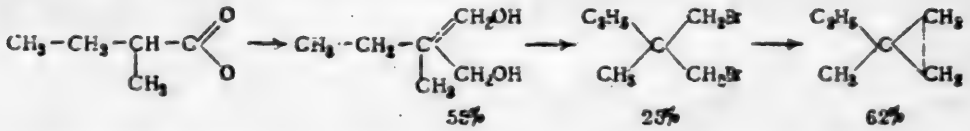
Ya. M. Slobodin, V. I. Grigoryeva and Ya. E. Shmulyakovsky

At the present time many hydrocarbons of the cyclopropane series are not readily accessible and have been inadequately investigated.

Below we describe the synthesis of 1-methyl-1-ethylcyclopropane and 1-methyl-1-isopropylcyclopropane which have not previously been prepared by a direct method.

Both hydrocarbons have been isolated from complex hydrocarbon mixtures formed by the action of zinc dust on 1,1,1-tribromotrimethylpropane and on 1,1,1-tribromotrimethyl-2-methylpropane [1]. The amount of these hydrocarbons in the mixtures resulting from dehalogenation is 3 and 5% respectively.

The starting material for synthesis of 1-methyl-1-ethylcyclopropane in our investigation was 2-methyl-1-butanal. Condensation of this aldehyde with formaldehyde in an alkaline medium gave a diol [2] which was converted with PBr_3 into the dibromide [3]. Cleavage of two bromines from the dibromide with zinc dust led to formation of the hydrocarbon.



The so-formed hydrocarbon was of satisfactory purity as shown by spectroscopic examination; it was not contaminated with unsaturated hydrocarbons. In the Raman spectrum of this hydrocarbon the cyclopropane ring was represented by the group of frequencies 850, 881, 934, 1236 and 3058 cm^{-1}.

The starting material for synthesis of 1-methyl-1-isopropylcyclopropane was 2,3-dimethyl-1-butanal which gave the required cycloparaffin by the same series of reactions.

The purity of the hydrocarbon was adequate. Spectroscopic examination showed it to be free from unsaturated hydrocarbons. Corresponding to the three-membered ring in the Raman spectrum of 1-methyl-1-isopropylcyclopropane were the frequencies 841, 849, 933, 1228, 1258, and 3063 cm^{-1}. Our method may be proposed as a general method of synthesis of 1,1-dialkylcyclopropanes.

EXPERIMENTAL

2-Methyl-2-ethylpropane-1,3-diol

The diol was prepared from 2-methylbutanal and formaldehyde [2]. In a three-necked flask fitted with stirrer, dropping funnel and reflux condenser was placed a solution of 17 g KOH in 75 ml alcohol. From the dropping funnel was slowly run in a mixture of 22 g 2-methylbutanal, 65 ml 28% formaldehyde and 30 ml alcohol. During the addition of the mixture the temperature in the flask was kept at 40°. After completion of the addition, the flask was heated to 80°. Stirring was continued for 18 hours at this temperature. The alcohol was then driven off and the residue extracted 5-6 hours with ether. The ethereal solution was dried, the ether was driven off, and the diol was distilled. The latter formed white, hygroscopic crystals with m.p. 43° and b.p. 111-114° (10 mm). Yield of diol, 55% of the theoretical.

Found %: C 59.96; H 11.53. $C_6H_{14}O_2$. Calculated %: C 61.01; H 11.95

2-Methyl-2-isopropylpropane-1,3-diol

Preparation was by the above-described method, using 46.4 g 2,3-dimethylbutanal, 60 ml alcohol, 130 ml

28%, formaldehyde and a solution of 35 g KOH in 150 ml alcohol. Yield of diol, 46% of the theoretical. B.p. 139-140° (24 mm); m.p. 56-57°.

Found %: C 62.40; H 12.30; $C_7H_{16}O_2$. Calculated %: C 63.55; H 12.22

1,3-Dibromo-2,2-dialkylpropanes

Into a flask fitted with a dropping funnel and reflux condenser was charged 0.25 mole diol, after which 0.25 mole PBr_3 was run in slowly, the flask being cooled with iced water [3]. After the PBr_3 had been added, the bath temperature was slowly raised to 100°, and then the water bath was replaced by an oil bath and the mixture heated for 18 hours at 150°. After cooling, the mass was poured into cold water. The dibromo compound was extracted with ether. The ethereal solution was washed with water, then with sodium carbonate solution and again with water, and dried over calcium chloride. The ether was driven off and the dibromo compound distilled in vacuum.

1,3-Dibromo-2-methyl-2-ethylpropane. Yield 28% of the theoretical. B.p. 78° at 5mm and 92° at 17 mm.

d_4^{25} 1.6078; n_D^{20} 1.5073; MR_D 45.14. Calc. MR_D 45.47. Found %: Br 65.32. $C_6H_{12}Br_2$. Calculated %: Br 65.55.

Raman Spectrum

185 (7), 242 (3), 312 (1), 336 (0.5), 371 (1 w), 430 (2 w), 444 (2 w), 501 (2), 595 (0.5), 636 (7), 655 (10), 695 (2), 736 (6), 778 (2), 826 (3), 858 (4), 888 (1 w), 928 (2), 999 (1), 1055 (1), 1172 (0.5), 1192 (0.5), 1263 (2), 1309 (0.5), 1341 (0.5), 1443 (0.5).

1,3-Dibromo-2-methyl-2-isopropylpropane. Yield 25% of the theoretical. B.p. 123-125° at 30 mm; d_4^{20} 1.5408; n_D^{20} 1.5073; MR_D 49.86. Calc. MR_D 49.89.

Found %: Br 62.26. $C_7H_{14}Br_2$. Calculated %: Br 62.01.

1-Methyl-3-ethylcyclopropane

Into a flask fitted with a reflux condenser were charged 31 g zinc dust, 45 ml alcohol and 5 ml water. The mixture was heated to the boil, and addition was then made through a dropping funnel of 14.5 g 1,3-dibromo-2-methyl-2-ethylpropane. Water at 70° was circulated through the reflux condenser. The vapor of the formed hydrocarbon passed without condensing through the reflux condenser and then entered a well-cooled coil and condensed in the receiver. The hydrocarbon was washed with water, dried over calcium chloride and distilled over sodium. Yield 62% of the theoretical.

B.p. 56.5-57°; d_4^{20} 0.7013; n_D^{20} 1.3888; MR_D 28.30.

C_6H_{12}. Calc. MR_D 28.40*.

Raman Spectrum

199 (0.5), 265 (0.5), 362 (1 w), 415 (1), 431 (1), 446 (1), 479 (4), 674 (10), 736 (1), 788 (1), 851 (1), 881 (6), 934 (7), 1000 (5), 1067 (4), 1115 (2), 1236 (3), 1285 (3), 1388 (1), 1435 (3), 1456 (3), 2933 (6), 2960 (6), 2994 (20), 3058 (5).

1-Methyl-1-isopropylcyclopropane

The hydrocarbon was prepared from 1,3-dibromo-2-methyl-2-isopropylpropane in the conditions described above. The reaction was carried out in a Wurtz flask; the hydrocarbon was progressively distilled off with the alcohol as formed. Loss of alcohol during the reaction was made good by addition from the dropping funnel. Yield 77% of theory.

B.p. 82°; d_4^{20} 0.7215; n_D^{20} 1.4000; MR_D 39.92; Calc. MR_D 40.02.

Found %: C 85.29; H 14.23. C_7H_{14}. Calculated %: C 85.62; H 14.38.

Raman Spectrum

271 (2 w), 309 (2 w), 348 (2), 372 (1), 392 (1), 489 (3), 501 (2), 649 (1), 663 (10), 715 (1), 778 (1 w), 841 (8), 849 (5), 933 (9), 1004 (6), 1040 (2) 1084 (2), 1124 (4), 1158 (1), 1196 (2), 1228 (1), 1258 (7), 1313 (3), 1358 (2), 1380 (2), 1425 (3), 1448 (6), 1461 (6), 2874 (10), 2902 (2), 2936 (4), 2960 (8), 2995 (8), 3083 (3).

*The increment for a three-membered ring is assumed to be 0.7.

SUMMARY

1-Methyl-1-ethylcyclopropane and 1-methyl-1-isopropylcyclopropane have been prepared for the first time by direct synthesis.

Data are given for the Raman spectra of the prepared hydrocarbons and the intermediate products of their synthesis.

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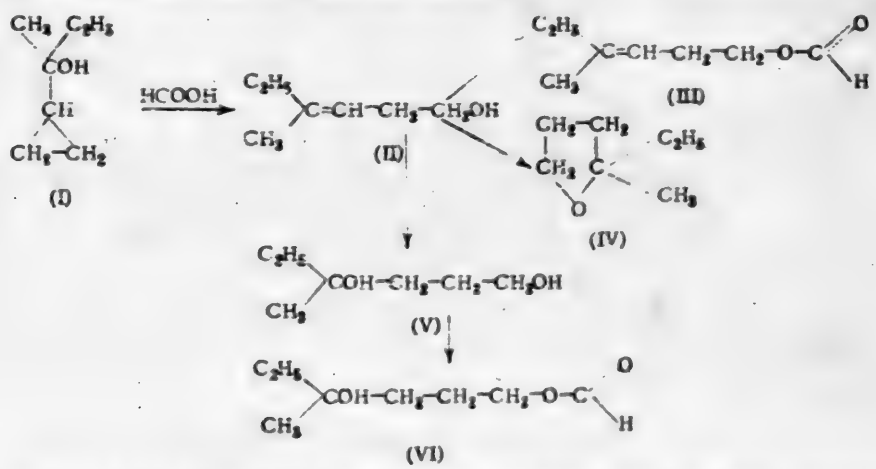
THE MECHANISM OF TRANSFORMATIONS OF TERTIARY ALCOHOLS OF THE CYCLOPROPANE SERIES UNDER THE INFLUENCE OF INORGANIC AND ORGANIC ACIDS

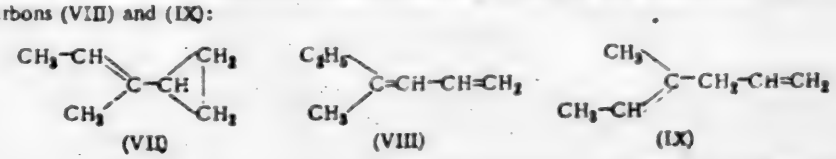
II. INTERACTION OF METHYLETHYLCYCLOPROPYLCARBINOL WITH DILUTE FORMIC ACID

T. A. Favorskaya and N. V. Shcherbinskaya

In collaboration with S. E. Chernobelskaya [1], we have studied the reaction of methylethylcyclopropylcarbinol with 80% formic acid; the sole product of this reaction was 2,2-methylethyltetrahydrofuran. In the present investigation we used more dilute acid in the dilution of 1:2 (pH 0.88) in order to have the possibility of obtaining intermediate products of the reaction and thus gaining an insight into its mechanism. The results that we obtained showed that in these conditions the interaction of methylethylcyclopropylcarbinol (I) with formic acid proceeds by the same mechanism as in the interaction of formic acid with dimethylcyclopropylcarbinol [2]: the hydroxyl group of the tertiary is shifted to the β-position while the three-membered ring is opened to form the unsaturated primary alcohol, 3-methyl-3-hexene-6-ol (II). This alcohol is then partly esterified with formation of the formic ester (III), partly isomerized to 2,2-methylethyltetrahydrofuran (IV), and to a small extent hydrogenated to α,α-methylethyltetramethylene glycol (V), which esterifies to the monoester (VI).



Moreover substitution of one methyl group of the alcohol by ethyl brings about still another direction of reaction—dehydration. This leads to formation of a mixture of hydrocarbons. The oxidation data showed that the mixture contains a cyclic hydrocarbon, dimethylcyclopropylethylene (VII), and also (apparently) the two isomeric unsaturated hydrocarbons (VIII) and (IX):

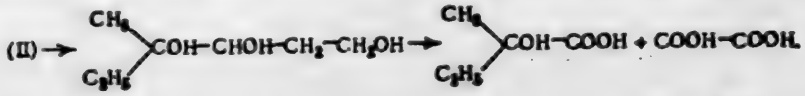


Here, as in the case of dimethylcyclopropylcarbinol, the formed unsaturated alcohol and its ester undergo conversion into an azeotropic mixture with b.p. 162-167°. Since isomeric transformations are possible in the hydrolysis of the esters, the mixture of alcohol and ester was treated with $MgICH_3$ for establishment of its structure. The reaction products were decomposed with water and sulfuric acid, dried and distilled in vacuum to give a primary alcohol —3-methyl-3-hexene-6-ol; on carrying out the distillation at normal pressure, however, the alcohol isomerizes to

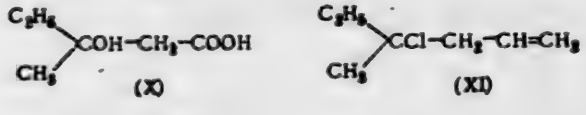
2,2-methylethyltetrahydrofuran. Decomposition of the reaction products with water alone followed by fractionation at the ordinary pressure gives the primary alcohol as the sole product. Negligible traces of sulfuric acid thus cause isomerization of the distilled alcohol to γ-oxide.

The yield of high-boiling fractions, corresponding to the glycol and its ester, is considerably lower than in the case of dimethylcyclopropylcarbinol; moreover, the formation of dienic hydrocarbons leads to polymeric products which contaminate the glycol and ester and still further reduce the yield. Hydrolysis of this mixture gave the glycol (V) in sufficiently pure form.

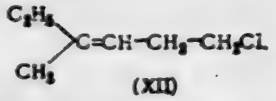
The mixture of alcohol (II) and ester (III) was oxidized with $KMnO_4$ solution; among other products of oxidation was found methylethylglycolic acid, whose formation may be represented by the scheme:



We obtained the same acid by oxidation of methylethylallylcarbinol and by oxidation of the unsaturated chloride formed from methylethylcyclopropylcarbinol by treatment with hydrochloric acid [3]. Oxidation of this chloride gave, apart from methylethylglycolic acid, methylethylethylenelactic acid (X). Methylethyl ketone was not obtained at all. The chloride was accordingly assumed to have the structure of 4-methyl-4-chloro-1-hexene (XI)



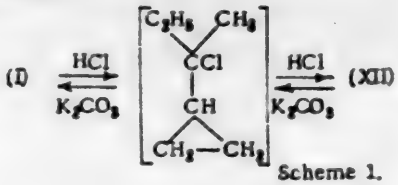
(X) (XI)



(XII)

Since the methylethylglycolic acid was obtained by oxidation of two differently constituted compounds and since the alcohol (one of the compounds in question) undoubtedly contains a double bond at the tertiary carbon atom, the question arises, first, whether the structure attributed to the chloride (XI) is correct, and, second, whether the method of oxidation with $KMnO_4$ solution can be applied to compounds containing a double bond at the tertiary carbon atom. With the aim of clarifying these problems, we performed a reaction of methylethylcyclopropylcarbinol with hydrochloric acid and ozonized the resultant chloride. In this manner we obtained methylethyl ketone and β-chloropropionic acid, thus showing conclusively that the chloride was primary and had the structure of 3-methyl-6-chloro-3-hexene (XII).

Consequently the interaction of methylethylcyclopropylcarbinol with hydrochloric acid proceeds similarly to the reaction of dimethylcyclopropylcarbinol and may be represented by scheme 1.



Scheme 1.

The formation of methylethylethylenelactic acid by oxidation of chloride (XII) indicates that in the conditions of oxidation with $KMnO_4$ solution the elements of hydrogen peroxide do not add on at the double bond but that hydration takes place, and therefore, this method is inapplicable to the determination of the structure of compounds containing a secondary-tertiary double bond. The ability of such a bond to be hydrated, which is now explained, confirms the theory—enunciated by us in a previous communication—that the formation of α,α-dimethyltetramethylene glycol by interaction of dimethylcyclopropylcarbinol with formic acid proceeds through addition of water to 2-methyl-2-penten-6-ol at the double bond. Such an interpretation of the reaction mechanism may also be applied to the formation of α,α-methylethyltetramethyleneglycol which is prepared by reaction of methylethylcyclopropylcarbinol with formic acid.

Since the iodide formed in the synthesis of methylethylcyclopropylcarbinol from ethylmagnesium iodide and acetyltrimethylene [3] gives, on oxidation with permanganate, the same acids as were formed from the chloride, while hydrolysis also gives the original cyclic alcohol, it is clear that the iodide is not 3-methyl-3-iodo-1-hexene, but a primary iodide with the structure of 3-methyl-6-iodo-1-hexene.

The action of organic acids on tertiary alcohols of the cyclopropane series results in the first place in formation of primary alcohol which then forms an ester; hence it may be suggested that the first step in the reaction with hydrogen halides is also formation of an unsaturated alcohol whose hydroxyl is then replaced by chlorine. In attempting, however, to prepare chloride (XI) by the action of HCl on alcohol (I), instead of the chloride we obtained a

tetrahydrofuran derivative, i.e. cyclization of the alcohol occurs under the influence of the acid medium, while the halogen derivative was only found in traces.

EXPERIMENTAL

1. Synthesis of Methylethylcyclopropylcarbinol

The carbinol was obtained by the action of ethylmagnesium bromide on acetyltrimethylene. The product had b.p. 138-144° and was oxidized by $KMnO_4$ in order to remove unsaturated impurities. Yield of alcohol with b.p. 141-143° was 54%. There was also obtained 8.6 g (about 5%) of a fraction with b.p. 70-72° at 17 mm and 170-172° at 760 mm, corresponding to the bromide with the constants:

n_D^{17} 1.4789; d_4^{17} 1.1763; MR_D 41.85. $C_7H_{13}Br$. Calculated: MR_D 41.83. Slabey's data [4]: n_4^{20} 1.4775; d_4^{20} 1.1873; b.p. 91-92° at 5 mm.

2. Interaction of Methylethylcyclopropylcarbinol with Formic Acid

150 g of the alcohol was heated to the boil while stirring for 1.5 hours with formic acid (1:2), i.e. approximately 38% (pH 0.88). After neutralization of the acid with dry sodium carbonate, extraction with ether and drying, the reaction products were fractionated in a column. The following fractions were isolated: 1st fraction, 102-107°, 29.4 g (23%); 2nd fraction, 107-112°, 6.5 g (5%); 3rd fraction, 119-122°, 14.5 g (9.6%); 4th fraction, 122-162°, 2.1 g (1.3%); 5th fraction, 162-167°, 57.0 g (30%). The residue in the flask, weighing 16.8 g, was fractionated in vacuum. Examination of first fraction with b.p. 102-107°. The fraction gave a reaction for the carbonyl group. A second fractionation in the column yielded a fraction with b.p. 104-106°. However, this fraction likewise gave traces of the 2,4-dinitrophenylhydrazone of acetyltrimethylene. For final purification, the compound was stood for several days over metallic Na and then refluxed with fresh Na for 3 hours on a funnel heater. A brown, gelatinous precipitate of the sodium derivative of the ketone separated. The liquid portion was drained and twice distilled over metallic Na. A second fractionation gave a fraction with b.p. 104-106°.

n_D^{15} 1.4430; d_4^{15} 0.7886; MR_D 32.27; C_7H_{12}. Calculated: MR_D 32.61; C_7H_{12}. Calculated: MR_D 33.69. Slabey's data [4] for the two isomeric cyclopropylbutenes: b.p. 106.55°; n_D^{20} 1.4428; d_4^{20} 0.7810; b.p. 107.46°; n_D^{20} 1.4474; d_4^{20} 0.7874.

Oxidation of the hydrocarbon. Oxidation of 7.3 g hydrocarbon required 23.1 g $KMnO_4$. The MnO_2 was drained and washed with hot water. The neutral products were driven off from the solution. The first drops of distillate gave a copious precipitate with 2,4-dinitrophenylhydrazine; m.p. 145° (from alcohol); no depression with the 2,4-dinitrophenylhydrazone of acetyltrimethylene. From the acidified solution were distilled the volatile acids; formic acid was detected in the distillate (qualitative test with $HgCl_2$). The solution of volatile acids was heated on a boiling water bath with excess of freshly precipitated silver carbonate. The precipitate was filtered and water was removed from the filtrate in vacuum. Analysis of the silver salts showed acetic acid to be present.

0.0705 g sub.: 0.0456 g Ag. Found %: Ag 64.68. $C_2H_3O_2Ag$. Calculated %: Ag 64.67.

From the aqueous solution of the nonvolatile acids was isolated oxalic acid; after several sublimations it had m.p. 185° and did not give a depression with authentic oxalic acid. The results show that the hydrocarbon with b.p. 104-106° is a mixture of hydrocarbons with an open chain and a three-membered ring.

The second fraction with b.p. 107-112° was acetyltrimethylene (2,4-dinitrophenylhydrazone with m.p. 146°).

The third fraction with b.p. 118-122° corresponded to 2,2-methylethyltetrahydrofuran. It was given a preliminary purification from acetyltrimethylene by heating with Na and by distillation over fresh Na.

n_D^{20} 1.4230; d_4^{20} 0.8593; MR_D 33.86. $C_7H_{14}O$. Calculated: MR_D 33.94. The constants agreed completely with those previously obtained by us [1].

Fraction 5 with b.p. 162-167°. Analyses showed this fraction to be a mixture of the primary alcohol 3-methyl-3-hexen-6-ol and its formate.

d_4^{20} 0.8932; n_D^{20} 1.4398; $C_8H_{14}O_2$ (calculated on the ester) MR_D 41.88. $C_7H_{14}O$ (calculated on the alcohol) MR_D 33.62. $C_8H_{14}O_2$. Calculated: MR_D 40.34. $C_7H_{14}O$. Calculated: MR_D 35.58.

0.1008 g sub.: 0.2573 g CO_2; 0.0998 g H_2O. Found %: C 69.61; H 11.07. $C_7H_{14}O$. Calculated %: C 73.62; H 12.35. $C_8H_{14}O_2$. Calculated %: C 67.57; H 9.92.

Hydrolysis of the mixture of alcohol and ester. 20 g substance was heated to boiling with twice the amount of 10% potassium carbonate solution with stirring. Hydrolysis was carried out for 15 hours. The product was extracted

with ether. After drying and driving off the solvent, a substance was obtained with b.p. 169-170°. Yield of alcohol 15 g.

d_4^{17} 0.8610; n_D^{17} 1.4510; MR_D 35.64. $C_5H_{10}O$. Calculated: MR_D 35.58. The constants agreed with our previous data [5].

0.1028 g sub.: 21.5 ml CH_4 (15.5°, 757 mm). OH number 0.988.

Oxidation of mixture of primary alcohol with its formic ester (b.p. 162-167°). Oxidation of 10 g substance consumed 37 g $KMnO_4$. The first drops of distillate of neutral products gave a precipitate with 2,4-dinitrophenylhydrazine with m.p. 116-117° (from alcohol). A mixed test with the 2,4-dinitrophenylhydrazone of authentic methylethyl ketone did not give a depression. Among the volatile acids was found formic acid. The non-volatile acids were extracted with ether in an extractor. After drying and driving off the ether, nearly the entire mass crystallized. The crystals were pressed on porous plate. Yield of acid 2 g; it was sublimed and recrystallized from benzene. M.p. 87°. No depression in test with authentic methylethylglycolic acid.

Action of $MgCH_2I$ on the mixture of primary alcohol and its ester. To the $MgCH_2I$ prepared from 3.5 g metallic Mg, 20.5 g CH_2I and 100 ml ether was added 12.5 g of the substance with m.p. 162-167° in 20 ml ether. The organo-Mg complex was decomposed with water and sulfuric acid (1:5). The reaction products were extracted with ether and dried with potassium carbonate. The ether extract was then divided into two parts. The first part, after driving off the ether, was distilled at normal pressure.

The first fraction, consisting of residues of ether and of formed isopropyl alcohol, came over at 40-115°, after which the temperature rose rapidly to 130° and then began to fall although material distilled over the whole time. The temperature fell to 120° and did not rise any higher. When the whole of the distillate was redistilled, it boiled at 120-122° and its constants corresponded to those of 2,2-methylethyltetrahydrofuran.

d_4^{20} 0.8603; n_D^{20} 1.4230; MR_D 33.74. $C_7H_{14}O$. Calculated: MR_D 33.94.

The second part, after removal of the ether, was distilled in vacuum to give a small fraction with b.p. up to 68° at 8 mm and a main fraction with b.p. 68-71° at 8 mm (n_D^{20} 1.4500), corresponding to 3-methyl-3-hexen-6-ol.

In a second experiment the organo-Mg complex was decomposed with water alone without addition of acid. The fractions so obtained were: 1) 50-160°; 2) 160-165° (a few drops); 3) 166-168°; yield 50.6%; n_D^{20} 1.4495.

Consequently, the isomerization of alcohol (I) to the tetrahydrofuran derivative requires traces of acid and heating to above 70°.

Examination of the high-boiling fractions. Repeated fractionations of the residue (16.8 g) in vacuum yielded a fraction with b.p. 112-114° at 14 mm. This was of the same order as the boiling point of the monoester of the glycol which we isolated after interaction of dimethylcyclopropylcarbinol with formic acid [2]. However, the analyses performed on the fraction with b.p. 112-114° at 14 mm showed that it was not a perfectly homogeneous substance although its boiling point did not change even after two more fractionations.

d_4^{20} 0.9667; n_D^{18} 1.4565; MR_D 45.01. $C_8H_{14}O_2$. Calculated: MR_D 42.45.

0.1065 g sub.: 0.2508 g CO_2; 0.1005 g H_2O. 0.1304 g sub.: 18.0 ml CH_4 (13.5°; 773 mm). Found %: C 64.20; H 10.5. OH number 0.9740. $C_8H_{14}O_2$. Calculated %: C 60.00; H 10.00; OH number 1.

Hydrolysis of substance with b.p. 112-114° at 10 mm. 4 g substance was heated with twice the amount of 20% potassium carbonate solution. The products of hydrolysis were extracted with ether. After drying and removal of the ether, the residue was distilled in vacuum to give 0.45 g viscous substance with b.p. 122-123° at 8 mm (n_D^{20} 1.4600). The aqueous solution was acidified with sulfuric acid and the volatile acids distilled with steam. Formic acid was detected in the distillate. The fraction with b.p. 122-123° at 8 mm is evidently methylethyltetramethylene glycol, but its minute amount prevented its further examination. For the purpose of identification the glycol was synthesized.

Synthesis of α-methyl-α-ethyltetramethylene glycol. To the ethyl magnesium bromide prepared from 12 g Mg and 54.5 g ethyl bromide was added 25.5 g acetopropyl alcohol dissolved in 50 ml ether. The organomagnesium complex was decomposed with water and NH_4Cl. The reaction products were extracted with ether. After drying, driving off the ether and distilling, a substance with b.p. 139-140° at 22 mm was obtained in a yield of 12 g (36%).

d_4^{20} 0.9713; n_D^{20} 1.4575; MR_D 37.62. $C_7H_{14}O_2$. Calculated: MR_D 37.82.

0.1331 g sub.: 0.3119 g CO_2; 0.1424 g H_2O. 0.0730 g sub.: 20.9 ml CH_4 (16°, 760 mm). Found %: C 63.30; H 11.97; OH number 2.066. $C_7H_{14}O_2$. Calculated %: C 63.63; H 12.12; OH number 2.

3. Interaction of 3-Methyl-3-hexen-6-ol with Hydrochloric Acid

6.3 g of the alcohol was stirred for 2 hours at room temperature with 24 ml hydrochloric acid in 1:1 dilution. The reaction product was extracted with ether and dried with potassium carbonate. Distillation gave two fractions: 1) 120-122°, 3.5 g (62%) and 2) 122-130°, 1.1 g. The first fraction is 2,2-methylethyltetrahydrofuran and the second is probably a mixture of the first fraction with traces of primary chloride since a Beilstein halogen test gave a positive result (b.p. of the chloride 154-156°).

4. Reaction of Methylethylcyclopropylcarbinol with Hydrochloric Acid

25 g of the alcohol was stirred at room temperature for 2 hours with 100 ml hydrochloric acid in 1:1 dilution. The upper layer was separated and dried with potassium carbonate. Fractionation gave 19 g of chloride with b.p. 154-156°, in agreement with our earlier data [3].

Ozonization of the chloride. 5 g chloride was ozonized in chloroform. After removal of the solvent, the ozonide was decomposed with water while heating on a water bath. The products of decomposition were extracted with ether; after drying and removing the solvent, a syrupy liquid remained, a portion of which was worked up with 2,4-dinitrophenylhydrazine solution to give an abundant yellow precipitate with m.p. 117° (from alcohol). A mixed melting point test with the 2,4-dinitrophenylhydrazone of methylethyl ketone did not give a depression. The remaining portion of the ozonization products was distilled in vacuum and gave a fraction with b.p. 102-105° at 23 mm which soon crystallized (m.p. 39°). The analysis corresponds to that of β-chloropropionic acid.

0.1066 g sub.: 0.1444 g AgCl. Found %: Cl 32.80. $C_3H_5O_2Cl$. Calculated %: Cl 32.71.

Ozonization did not yield any products other than methylethyl ketone and β-chloropropionic acid.

SUMMARY

1. The interaction of methylethylcyclopropylcarbinol with formic acid (pH 0.88) was studied.

2. It was established that this reaction proceeds in a similar manner to the reaction of formic acid with dimethylcyclopropylcarbinol; it differs from the latter, however, in that a mixture of hydrocarbons is also formed.

3. In addition to the hydrocarbons, the reaction gives 5 substances: a primary alcohol—3-methyl-3-hexen-1-ol—and its formic ester; 2,2-methylethyltetrahydrofuran; α,α-methylethyltetramethylene glycol; and the partial formic ester of the glycol.

4. It was established that the product of reaction of methylethylcyclopropylcarbinol with hydrochloric acid is the unsaturated primary chloride, 3-methyl-6-chloro-3-hexene, whose structure was confirmed by ozonization.

5. It was established that the method of oxidation with $KMnO_4$ solution of compounds containing a secondary-tertiary double bond does not give accurate results.

6. The glycol, 3-methylhexane-3,6-diol, was synthesized for the first time.

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* See Consultants Bureau English translation, page 891.

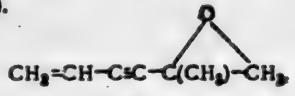
** See Consultants Bureau English translation, page 1553.

*** See Consultants Bureau English translation, page 437.

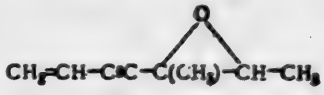
ADDITION OF AMMONIA AND DIETHYLAMINE TO OXIDES OF THE VINYLACETYLENE SERIES

F. Ya. Perveev and N. I. Kudryashova

Numerous investigations have been devoted [1] to the addition of ammonia and amines to olefinic α-oxides; up to now, however, the addition of ammonia and amines to α-oxides of the vinylacetylenic series has not been studied. We considered it was necessary to study the influence of the vinylacetylene radical upon both the reactivity of oxides and the order of addition of ammonia. The compounds investigated were 2-methyl-oxido-1,2-hexen-5-yne-3 (I), 3-methyl-oxido-2,3-hepten-6-yne-4 (II) [2] and, for comparison, the saturated oxide, 2-methyl-oxido-1,2-hexane (III).



(I)



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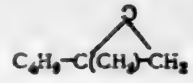

(III)

In the reaction of the oxides with ammonia, it was established that the velocity of addition of ammonia depends on the structural features of the oxides. For example, with oxide (I) at the ordinary temperature the reaction is completed in 8 hours. In these conditions oxide (II) reacted only to the extent of 50% in 8 days. The saturated oxide (III) practically does not react at room temperature. The reaction proceeds to completion only on heating in a sealed tube for 20-25 hours at 100°.

The addition of diethylamine to oxide (I) proceeds slowly more than that of ammonia (over a period of 46 hours, 1/3 of the original amount of oxide reacted). Addition of alkaline catalysts has practically no influence on the rate of addition of ammonia and diethylamine.

The following method was adopted for preparation of the aminoalcohols: To a 33% aqueous solution of ammonia (5-fold excess) with continuous stirring at room temperature was added the oxide. The duration of stirring was mentioned above. In the absence of intensive stirring, the unsaturated oxides react with ammonia to form resins, and hydroxyamines could not be isolated.

The physical constants of the prepared compounds are set forth in the table.

The prepared unsaturated hydroxyamines are liquids with an unpleasant odor, readily soluble in water, ether and alcohol; they polymerize even when kept in a sealed tube. 1-Amino-2-methyl-2-hydroxyhexene-5-yne-3 (I') crystallizes on keeping (m.p. 44.5-45.5°).

The prepared hydroxyamines are thermally unstable; they decompose completely when heated in a vacuum at above 140°; they do not form picrates.

1-Amino-2-methyl-2-hydroxy-hexen-5-yne-3 (I') is completely hydrogenated over Raney nickel in an autoclave at a pressure of 122 atm. and a temperature of 50-55°. At the ordinary temperature and pressure hydrogenation over Raney nickel proceeds very sluggishly.

Reaction of $C_4H_9-\underset{\displaystyle CH_3}{\overset{\displaystyle |}{C}}(OH)-CH_2NH_2$ with α-naphthylisocyanate gives a crystalline product with m.p. 115-116° (a urea derivative). A mixed melting test of the urea derivatives prepared from the product of hydrogenation of the unsaturated hydroxyamine and the saturated aminoalcohol (III') did not give a depression.

The identity of the physical constants of the product of hydrogenation and those of 1-amino-2-methyl-hexanol-2 and the absence of a depression in the mixed melting test are evidence of the identity between the two substances. On this basis we may assume that the addition of ammonia to unsaturated oxides follows the K. A. Krasusky

Formula	B.p. (°C)	n_D^{20}	d_4^{20}	MR_D	
				Calculated	Found
I'. $CH_2=CH-C\equiv C-C(OH)(CH_3)-CH_2NH_2$	91-92 (4 mm)	1.5165	1.0078	36.4	37.5
II'. $CH_2=CH-C\equiv C-C(OH)(CH_3)-CHNH_2-CH_3$	97-98 (7 mm)	1.5061	0.9771	41.62	42.47
III' $C_4H_9-C(OH)(CH_3)-CH_2NH_2$	85-86 (7 mm)	1.4640	0.9045	39.47	39.29
IV. Product of complete hydrogenation of (I').	69-70 (3 mm)	1.4545	0.9095	39.47	39.11
V $CH_2=CH-C\equiv C-C(OH)(CH_3)-CH_2N(C_2H_5)_2$	92-93 (7 mm)	1.4762	0.8915	55.99	57.36

rule [4] (the oxide ring is broken at the most hydrogenated atom of carbon)

The saturated oxide (III) was synthesized by the Grignard method by the action of chloroacetone on butylmagnesium bromide. The chloroacetone was added quickly to the reaction mixture in the course of a few minutes with cooling to −10 to −12°. Slow addition of the chloroacetone with less intensive cooling leads predominately to an alcohol with high molecular weight [3].

EXPERIMENTAL

Preparation of 1-Amino-2-methyl-2 hydroxyhexen 5-yne 3 (I')

200 ml 33% aqueous solution of ammonia was placed in a round-bottomed flask fitted with mechanical stirrer and mercury seal. Addition was then made of 25 g 2-methyl-oxido-1,2-hexen-5-yne-3 [2]. The reaction mixture was stirred for several hours at room temperature. The reaction was assumed to be at an end when the oxide had completely dissolved. The water and excess ammonia were taken off in vacuum and the residual dark-brown liquid dissolved in ether. The ethereal solution was dried with $MgSO_4$, the ether was removed, and the product distilled in vacuum. Yield 20 g hydroxyamine (69%).

0.2680, 0.2729 g substance: 24.6, 24.8 ml N_2 (16°, 766.8 mm). 0.1379, 0.1151 g substance: 58.1, 47.7 ml CH_4 (14.5°, 761.8 mm). Found %: N 10.8, 10.7 active H 1.739, 1.750. $C_7H_{13}ON$. Calculated %: N 11.19; active H 1.613

Hydrogenation. 9.5 g hydroxyamine was dissolved in methyl alcohol and hydrogenated over Raney nickel in a rotating autoclave (volume 350 ml) at 50-55° and an initial pressure of 122 atm. After 4 hours' hydrogenation the pressure had dropped to 91 atm., and it then remained constant for an hour. Hydrogen absorption was 10,850 ml. Hydrogenation of the double and triple bond requires 10,500 ml hydrogen

After driving off the methyl alcohol, the product was dried and distilled in vacuum.

0.1521, 0.1439 g substance: 14.25, 13.4 ml N_2 (18°, 761.8 mm). Found %: N 10.88, 10.83. $C_7H_{17}ON$. Calculated %: N 9.68.

With α-naphthylisocyanate in ligroine the substance forms a crystalline urea derivative. After recrystallization from benzene the white crystals had m.p. 115-116°.

0.1208, 0.1282 g substance: 10.0 ml N_2 (19°, 760 mm), 10.35 ml N_2 (18°, 763.3 mm). Found %: N 9.55, 9.40. $C_{18}H_{24}O_2N_2$. Calculated %: N 9.33.

Preparation of 2-Amino-3-methyl-3-hydroxyhepten-6-yne 4 (II')

The reaction was conducted as described above.

Reactants were 100 ml 33% aqueous ammonia and 10 g 3-methyl-oxido 2,3-hepten-6-yne-4. Stirring was continued for 8 days. Yield 5 g (43%) hydroxyamine.

0.1318, 0.1401 g substance: 11.8, 12.7 ml N_2 (18°, 747.1 mm). 0.1175 g substance: 41.8 ml CH_4 (18°, 747.1 mm). Found %: N 10.21, 10.33; active H 1.463. $C_8H_{13}ON$. Calculated %: N 10.06; active H 1.448.

Preparation of 2-Methyl-oxido-1,2-hexane (III)

To 0.75 mole butylmagnesium bromide in ethereal solution was added, with stirring and cooling, 60 g chloroacetone over a period of 9 hours. After decomposition with 30% acetic acid, the ethereal solution was separated and dried with $MgSO_4$; the ether was removed and the residue distilled in vacuum (5 mm) at 66-67°.

n_D^{25} 1.4500; d_4^{25} 1.0043. Found: MR_D 40.3. $C_7H_{15}OCl$. Calculated: MR_D 40.92.

0.2831, 0.2717 g substance: 0.2777, 0.2575 g AgCl. Found %: Cl 23.39, 23.45. $C_7H_{15}OCl$. Calculated %: Cl 23.53.

The prepared chlorhydrin was dissolved in ether and by treatment with pulverized KOH gave the oxide (III) with b.p. 135-136° at 762 mm.

n_D^{20} 1.4111; d_4^{20} 0.8304. Found MR_D 34.15. $C_7H_{14}O$. Calculated MR_D 33.97.

0.1018, 0.1032 g substance: 0.2742, 0.2775 g CO_2; 0.1146, 0.1149 g H_2O. Found %: C 73.51, 73.39; H 12.60, 12.45. $C_7H_{14}O$. Calculated %: C 73.63; H 12.36.

Preparation of 2-Methyl-2-butyl-2-hydroxyethylamine (III')

A mixture of 20 g of the saturated oxide (III) and 60 ml 35% aqueous ammonia in a sealed tube was heated at 100° for 20-25 hours. After driving off the excess of ammonia and water, 8 g aminoalcohol was isolated.

0.1350 g substance: 12.7 ml N_2 (17°, 759.2 mm). 0.1435 g substance: 54.4 ml CH_4 (15.5°, 757.8 mm). Found %: N 10.78; active H 1.595. $C_7H_{17}ON$. Calculated %: N 10.68; active H 1.536.

Reaction of α-naphthylisocyanate in ligroine with the hydroxyamine gave a urea derivative—a crystalline substance with m.p. 109-110° (from benzene).

Condensation of 2-Methyl-oxido-1,2-hexen-5-yne-3 (I) with Diethylamine

To an aqueous solution of 50 ml diethylamine was added 15 g oxide (I). The mixture was left for 46 hours at room temperature and shaken from time to time. 6 g unreacted oxide and 10 g tertiary aminoalcohol (V) were isolated. When the oxide was kept in contact with diethylamine for 96 hours, the yield of aminoalcohol increases to 85.8%.

0.1535 g substance: 20.6 ml CH_4 (15°, 767.3 mm). 0.2107 g substance: 13.2 ml N_2 (16°, 762.4 mm). Found %: active H 0.570; N 7.76. $C_{11}H_{23}ON$. Calculated %: active H 0.556; N 7.73.

SUMMARY

1. Reaction of the oxides 2-methyl-oxido-1,2-hexen-5-yne-3 and 3-methyl-oxido-2,3 hepten-6-yne-4 with ammonia gave the aminoalcohols: 1-amino-2-methyl-2-hydroxy-hexen-5-yne-3 and 2-amino-3-methyl-3-hydroxy-hepten-6-yne-4.

2. Reaction of 2-methyl oxido-1,2-hexen-5-yne-3 with diethylamine gave a tertiary aminoalcohol of the vinylacetylenic series.

3. It was established that the velocity of addition of ammonia in the given conditions depends on the structural characteristics of the oxides.

4. On the model of 1-amino-2-methyl-2-hydroxyhexen-5-yne 3 it was shown that ammonia adds on to oxides of the vinylacetylenic series according to the K. A. Krasusky rule.

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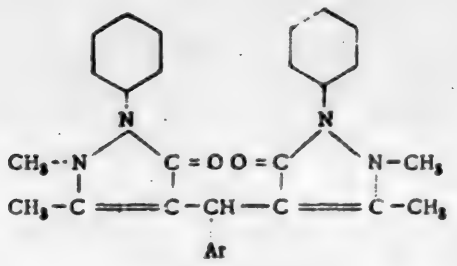
* See Consultants Bureau English translation, page 1623

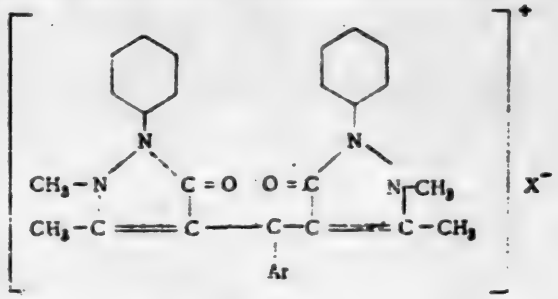
DYES CONTAINING ANTIPYRINE NUCLEI. III

O. F. Ginzburg

Interaction of antipyrine with benzaldehyde is known to give diantipyrylphenylmethane [1]. Experiments showed that also other aromatic aldehydes, such as o-, m-, and p-nitrobenzaldehydes, α-naphthaldehydes, p-chlorobenzaldehyde and vanillin, in aqueous or aqueous-alcoholic solutions in presence of hydrochloric acid react with antipyrine to form compounds of the diantipyrylarylmethane series (I). Like diantipyrylphenylmethane [2], these compounds are leuco bases of dyes (II), similar in structure and properties to the basic triphenylmethane dyes.

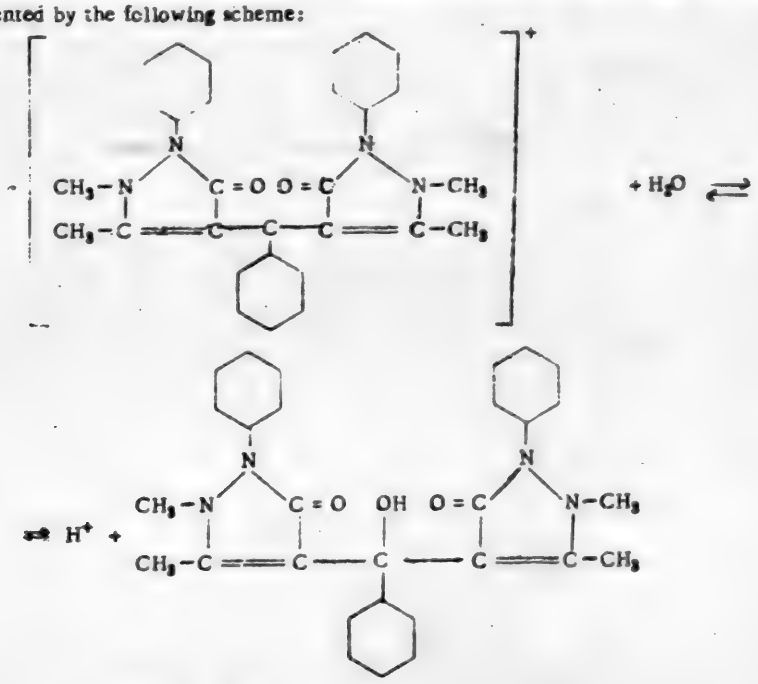


(I)



(II)

Dyes containing antipyrine nuclei are salts and resemble the basic triphenylmethane dyes [3] in undergoing hydrolysis in aqueous solutions. In the case of the dye known as antipyrine orange, to take an example, this hydrolysis may be represented by the following scheme:



(III)

A study of the acid-base equilibrium in aqueous solutions of dyes containing antipyrine nuclei enabled determination of their hydrolysis constants (K_h) and in turn of the dissociation constants (K_a) of the carbonyl compounds formed from these dyes. The data are set forth in Table 1.

TABLE 1

Name of compound	K_a*
Diantipyrylphenylcarbinol [3]	$2.88 \cdot 10^{-8}$
Diantipyryl-p-chlorophenylcarbinol	$1.05 \cdot 10^{-8}$
Diantipyryl-p-nitrophenylcarbinol	$3.17 \cdot 10^{-10}$

Examination of the tabulated data shows that the introduction into the phenyl group in the para-position to the central carbon atom of a nitro group or of a chlorine atom very considerably lowers the basicity of the carbinol and, consequently, increases the hydrolysis of the corresponding dye. It is also noteworthy that although the basicity of diantipyryl-p-chlorophenylcarbinol is higher than that of diantipyryl-p-nitrophenylcarbinol, the dye formed from the latter has a rather deeper color (Fig. 1, curve a) than the dye obtained from diantipyryl-p-chlorophenylcarbinol (Fig. 1, curve b). A study was also made of the hydrolysis of dyes containing antipyrine nuclei in 60% aqueous acetone.

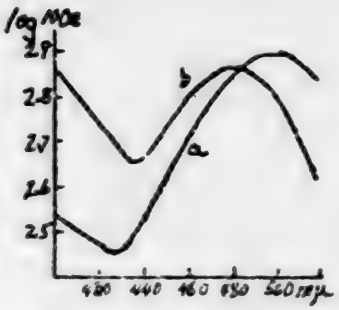


Fig. 1.

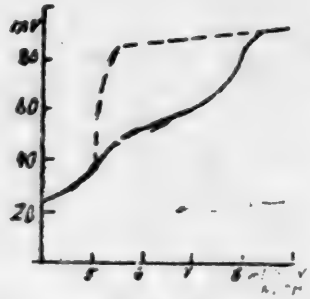


Fig. 2.

The data set forth in Tables 2 and 3 show that hydrolysis of the dyes in 60% aqueous acetone is approximately 10 times greater than in water.

As was already noted in the previous communication [2], addition of caustic alkali solution to a solution of dyes containing antipyrine nuclei is accompanied by the phenomenon of "slow neutralization". In Fig. 2 is plotted the change of pH of the solution observed on adding 0.1 N NaOH to a solution of antipyrine orange. The upper curve characterizes the pH of the solution observed immediately after addition of each portion of alkali; the lower one shows the pH of the solution after 20 minutes. The change of pH of the solution, as follows from inspection of equation (III), is associated with the establishment of equilibrium in the solution.

EXPERIMENTAL

1. Diantipyryl-o-nitrophenylmethane

Base. To a solution of 3.76 g antipyrine (0.02 mole) and 1.51 g o-nitrobenzaldehyde (0.01 mole) in 15 ml alcohol is added 8 ml hydrochloric acid (sp.gr.1.17). After an hour 25 ml water is added and the alcohol is driven off by heating. The following day the reaction mass is diluted with twice the amount of water. A precipitate rapidly forms and the whole mass thickens. The precipitate is filtered off and treated with dilute sodium carbonate solution while heating. 3.50 g base with m.p. 207-209° is obtained. Yield 69% of the theoretical. After two crystallizations from toluene the m.p. is 214-215°. Further crystallization did not raise the melting point.

0.1185 g substance: 14.3 ml N_2 (18°, 760 mm). 0.1259 g substance: 15.2 ml N_2 (18°, 759 mm). 0.1322 g substance: 0.3321 g CO_2; 0.0647 g H_2O. Found %: C 68.50; H 5.48; N 13.82, 13.93. $C_{29}H_{27}O_4N$. Calculated %: C 68.35; H 5.34; N 13.78.

Hydrochloride. This salt crystallizes from 3% hydrochloric acid. M.p. (with decomposition) 125-126°.

The hydrogen chloride content of the salt is determined in all the experiments by potentiometric titration of the aqueous acetone solution.

0.1470 g substance. 2.65 ml 0.1 N NaOH. 0.1531 g substance: 2.89 ml 0.1 N NaOH (T 0.00401). Found %: HCl 6.58, 6.89. $C_{29}H_{27}O_4N_3 \cdot HCl$. Calculated %: HCl 6.69.

The picrate of the base crystallizes from alcohol; m.p. 163-164°.

* The data are mean values of several experiments.

0.0961 g substance: 12.6 ml N_2 (20°, 762 mm). 0.0997 g substance: 13.3 ml N_2 (20°, 760 mm). Found %: N 15.08, 15.54. $C_{29}H_{27}O_4N_5 \cdot C_6H_3O_7N_3$. Calculated %: N 15.17.

2. Diantipyryl-m-nitrophenylmethane*

The base is prepared by the same method as for diantipyryl-o-nitrophenylmethane. Yield 97% of the theoretical. After crystallization from toluene, m.p. 214°.

0.1380 g substance: 0.3468 g CO_2; 0.0663 g H_2O. 0.1290 g substance: 0.3228 g CO_2; 0.0623 g H_2O. 0.1265 g substance: 15.1 ml N_2 (20°, 758 mm). Found %: C 68.58, 68.29; H 5.38, 5.40; N 13.66. $C_{29}H_{27}O_4N_5$. Calculated %: C 68.35; H 5.34; N 13.78.

Hydrochloride. Crystallizes from 3% hydrochloric acid. M.p. with decomposition at 179-180°.

0.0977 g substance: 10.4 ml N_2 (23°, 755 mm). 0.9486 g substance: 0.2278 g AgCl. 0.3018 g substance: 5.21 ml NaOH (T 0.00404). Found %: N 12.20; Cl 5.95; HCl 6.38. $C_{29}H_{27}O_4N_5 \cdot 2H_2O \cdot HCl$. Calculated %: N 12.03; Cl 6.09; HCl 6.27.

Picrate of the base. M.p. 237° (from alcohol).

0.1511 g substance: 17.2 ml N_2 (16°, 751 mm). 0.1148 g substance: 15.3 ml N_2 (17°, 751 mm). Found %: N 15.11, 15.28. $C_{29}H_{27}O_4N_5 \cdot C_6H_3O_7N_3$. Calculated %: N 15.17.

3. Diantipyryl-α-naphthylmethane**

The procedure was the same as for diantipyryl-o-nitrophenylmethane. Yield 92.5% of the theoretical. After crystallization from toluene, alcohol or acetone, m.p. 254°.

0.1123 g substance: 10.7 ml N_2 (23°, 760 mm). Found: M 520.5; %: N 10.87. $C_{33}H_{30}O_2N_4$. Calculated: M 514.6; %: N 10.88.

4. Diantipyryl-p-nitrophenylmethane

Base. To a solution of 10.28 g antipyrine (0.06 mole) in 20 ml concentrated hydrochloric acid (spgr. 1.18) is added a solution of 4.56 g p-nitrobenzaldehyde (0.03 mole) in 15 ml alcohol. The next day the precipitate is filtered, 30 ml water is added to the filtrate and the alcohol is driven off. An additional amount of salt comes down and is combined with the first portion. The salt is decomposed with dilute NaOH solution and 11.32 g base is obtained or 74.6% of the theoretical. M.p. 232° (from alcohol).

0.1163 g substance: 0.2921 g CO_2; 0.0568 g H_2O. 0.1300 g substance: 15.9 ml N_2 (21°, 752 mm). 0.1189 g substance: 14.5 ml N_2 (21°, 752 mm). Found %: C 68.51; H 5.47; N 13.76; 13.71. $C_{29}H_{27}O_4N_5$. Calculated %: C 68.35; H 5.34; N 13.78.

Hydrochloride. Crystallizes from 3% hydrochloric acid. Melts with decomposition at 218-221°.

0.1913 g substance: 3.42 ml 0.1 N NaOH. 0.2061 g substance: 3.71 ml 0.1 N NaOH (T 0.00408). Found %: HCl 6.66, 6.70. $C_{29}H_{27}O_4N_5 \cdot HCl$. Calculated %: HCl 6.69.

Picrate of the base. M.p. 248-249° (from alcohol). 0.1161 g substance: 15.4 ml N_2 (20°, 763 mm). 0.1211 g substance: 16.2 ml N_2 (20°, 762 mm). Found %: N 15.18, 15.38. $C_{29}H_{27}O_4N_5 \cdot C_6H_3O_7N_3$. Calculated %: N 15.17.

5. Diantipyryl-p-chlorophenylmethane

The base is prepared as in the case of diantipyryl-p-nitrophenylmethane. Yield 66.3% of the theoretical. After crystallization from toluene-ligroine (1 : 4), m.p. 169°.

0.1281 g substance: 12.6 ml N_2 (20°, 762 mm). 0.1139 g substance: 11.3 ml N_2 (20°, 762 mm). 0.1315 g substance: 0.3361 g CO_2; 0.0661 g H_2O. Found %: C 69.70; H 5.63; N 11.37, 11.47. $C_{29}H_{27}O_2N_4Cl$. Calculated %: C 69.81; H 5.46; N 11.24.

The hydrochloride crystallizes from 3% hydrochloric acid. M.p. with decomposition 201-203°.

0.1400 g substance: 2.50 ml 0.1 N NaOH. 0.1731 g substance: 3.08 ml 0.1 N NaOH (T 0.00408). Found %: HCl 6.83, 6.63. $C_{29}H_{27}O_2N_4Cl \cdot HCl$. Calculated %: HCl 6.82.

*The preparation was carried out in collaboration with Z. Kh. Markazen.

**Preparation of diantipyryl-α-naphthylmethane and of the picrate of diantipyryl-α-naphthylcarbinol was carried out in collaboration with R. Ya. Selezneva.

Picrate of the base. M.p. 218-220° (from alcohol).

0.1095 g substance: 13.0 ml N_2 (23°, 765 mm). 0.1125 g substance: 13.1 ml N_2 (23°, 764 mm). Found %: N 13.65, 13.50. $C_{29}H_{27}O_2N_4Cl \cdot C_6H_3O_7N_3$. Calculated %: N 13.47.

6. Diantipyryl-m-methoxy-p-hydroxyphenylmethane

Base. To a solution of 3.76 g antipyrine (0.02 mole) in 15 ml hydrochloric acid (sp. gr. 1.18) is added 1.52 g (0.01 mole) vanillin. The latter dissolves quickly. After 30 minutes 15 ml water is added. The next day the precipitate is filtered off, and dissolved in 800 ml hot water. To the resultant solution is added 20 ml 20% sodium acetate solution. The white precipitate is filtered and dried. 4.85 g base is obtained or 95% of the theoretical. After two crystallizations from 50% alcohol, m.p. 146-148°.

0.1035 g substance: 9.9 ml N_2 (20°, 755 mm). 0.1112 g substance: 10.8 ml N_2 (20°, 756 mm). 0.1318 g substance: 0.3402 g CO_2; 0.0709 g H_2O. Found %: C 70.25; H 6.16; N 10.97, 11.15. $C_{30}H_{30}O_4N_4$. Calculated %: C 70.58; H 5.92; N 10.97.

Hydrochloride. It crystallizes from 2.5% hydrochloric acid. M.p. with decomposition 125-126°

0.2555 g substance: 4.70 ml 0.1 N NaOH (T 0.00400). 0.2649 g substance: 4.81 ml 0.1 N NaOH (T 0.00400) Found %: HCl 6.71, 6.67. $C_{30}H_{30}O_4N_4 \cdot HCl$. Calculated %: HCl 6.67.

Picrate. M.p. 208-209° (from alcohol).

0.1013 g substance: 11.8 ml N_2 (22°, 765 mm). 0.1216 g substance: 14.0 ml N_2 (21°, 765 mm). Found %: N 13.45, 13.33. $C_{30}H_{30}O_4N_4 \cdot C_6H_3O_7N_3$. Calculated %: N 13.31.

7. Oxidation of the Leuco Bases to Dyes

0.05 g leuco base is dissolved by heating in 1-2 ml 15% hydrochloric acid and to the boiling solution is added a few crystals of sodium nitrite. The solution acquires a deep-orange color. Formation of dyes is observed on oxidizing the following leuco bases: diantipyrylphenylmethane, diantipyryl-o-nitrophenylmethane, diantipyryl-m-nitrophenylmethane, diantipyryl-p-nitrophenylmethane, diantipyryl-p-chlorophenylmethane, diantipyryl-m-methoxy-p-hydroxyphenylmethane, and diantipyryl-α-naphthylmethane.

8. Diantipyryl-p-nitrophenylcarbinol

5 g diantipyryl-p-nitrophenylmethane hydrochloride is dissolved with heating in 50 ml concentrated hydrochloric acid. To the hot solution is added 0.5 g sodium nitrite in small portions over a period of 3-4 minutes, followed by 1.2 ml nitric acid (sp. gr. 1.4) dropwise over a period of 10 minutes. After addition of the whole of the nitric acid, the solution is boiled for 5-6 minutes and poured into 150 ml water. The orange solution is filtered and to the filtrate is added 15% NaOH solution until a precipitate appears. Dropwise addition is then made over a period of two hours of 2% NaOH solution until the reaction is alkaline to phenolphthalein. The next day the solution with precipitate is heated to the boil. After cooling, the precipitate is filtered and dried. Yield 2.95 g base. After crystallization from benzene-gasoline (1 : 5) the m.p. is 180-181°.

0.1077 g substance: 12.5 ml N_2 (25°, 768 mm). 0.1102 g substance: 12.9 ml N_2 (25°, 768 mm). 0.1201 g substance: 0.2923 g CO_2; 0.0579 g H_2O. Found %: C 66.37; H 5.40; N 13.36, 13.41. $C_{29}H_{27}O_5N_5$. Calculated %: C 66.24; H 5.17; N 13.31.

Picrate. M.p. 130-133° (from alcohol).

0.1121 g substance: 15.0 ml N_2 (21°, 752 mm). 0.1183 g substance: 15.9 ml N_2 (20°, 750 mm). Found %: N 15.23, 15.31. $C_{29}H_{27}O_4N_5 \cdot C_6H_3O_7N_3$. Calculated %: N 15.20.

9. Diantipyryl-p-chlorophenylcarbinol

The preparation is by the same procedure as for diantipyryl p-nitrophenylcarbinol. Crystallizes from benzene-gasoline (1 : 5). M.p. 137-139°.

0.1239 g substance: 11.7 ml N_2 (20°, 759 mm). 0.1268 g substance: 12.1 ml N_2 (20°, 757 mm). 0.1086 g substance: 0.2689 g CO_2; 0.0526 g H_2O. Found %: C 67.49; H 5.54, N 10.89, 10.93. $C_{29}H_{27}O_3N_4Cl$. Calculated %: C 67.64; H 5.28; N 10.87.

10. Picrate of Diantipyryl-α-naphthylcarbinol

The oxidation of diantipyryl-α-naphthylmethane is performed in the same manner as that of diantipyryl-p-nitrophenylmethane. From 8 g diantipyryl-α-naphthylmethane is obtained 3.12 g crude base.

TABLE 2

Name of compound	Weight of sample (g)	0.1 N HCl (in ml) used in titration	0.1 N HCl (in ml) required by calculation	pH of solution of equimolar mixture of dye and carbinol	K_h
Diantipyryl-p-chlorophenylcarbinol	0.1049	2.02	2.04	6.10	$7.95 \cdot 10^{-7}$
Diantipyryl-p-nitrophenylcarbinol	0.1592	3.03	3.04	4.62	$2.40 \cdot 10^{-5}$

TABLE 3

Name of compound	Wt. of sample (in g)	0.1 N HCl solution (in ml)	pH of solution	K_h
Diantipyryl-p-chlorophenylcarbinol	0.0872	0.85	5.35	$8.92 \cdot 10^{-6}$
Diantipyryl-p-nitrophenylcarbinol	0.1612	1.54	3.70	$1.98 \cdot 10^{-4}$

To a hot solution of 2 g of the base in 60 ml alcohol is added 0.9 g picric acid in 20 ml alcohol. The next day the red crystals are filtered off, washed with a little alcohol and dried at 90-100°. Yield 1.9 g picrate with m.p. 235-236°. Further crystallizations did not change the melting point.

0.1040 g substance: 12.1 ml N_2 (21°, 756 mm). 0.1069 g substance: 12.4 ml N_2 (21°, 756 mm). Found %: N 13.33, 13.29. $C_{39}H_{31}O_9N_7$. Calculated %: N 13.22.

11. Study of Dissociation of the Carbonyl Compounds

a) A weighed amount of the carbinol is dissolved in a few ml 0.1 N hydrochloric acid and the solution made up to a volume of 200 ml. To the prepared solution of the dye is added 0.1 N NaOH solution in quantity sufficient for transformation of the dye into the carbinol compound. The solution gradually decolorizes. The obtained carbinol base remains in solution. After an hour the titration is performed. Readings are taken every 4-5 minutes after addition of each portion of hydrochloric acid. The titrated solution is at a temperature of 19°. The data are set forth in Table 2.

b) 0.1293 g diantipyryl-p-chlorophenylcarbinol is dissolved in 8.00 ml 0.1 N hydrochloric acid solution (T 0.00365) and the solution is mixed with 192 ml water. To the obtained hydrochloric acid solution of the dye is added 6.72 ml 0.1 N NaOH solution (T 0.00402). The pH of the solution is measured after 2 hours. The pH of the equimolar mixture of the dye and the carbinol is 6.15 (t 19°); K_h $1.11 \cdot 10^{-6}$.

c) A solution of 0.1761 g diantipyryl-p-nitrophenylcarbinol in 6.10 ml 0.1 N hydrochloric acid (T 0.00365) is mixed with 194 ml water. The solution is potentiometrically titrated. Temperature of solution, 19°. Readings are taken on the average every 4-5 minutes after addition of the particular portion of NaOH solution. With progressive addition of NaOH solution the solution loses color and by the end of the titration it is colorless. The formed diantipyryl-p-nitrophenylcarbinol remains in solution. Formation of diantipyryl-p-nitrophenylcarbinol required 3.36 ml 0.1 N NaOH (T 0.00402). The calculated amount of NaOH solution with T 0.00402 is 3.34 ml; the pH of the equimolar mixture of dye and carbinol is 4.60. Dissociation constant at K_h $3.16 \cdot 10^{-10}$.

d) A weighed amount of carbinol is dissolved in 70 ml 60% aqueous acetone. To the obtained solution is added 0.5 equivalent of 0.1 N hydrochloric acid solution (T 0.00365). The pH of the solution is measured after 2 hours (t 19°). The data are set forth in Table 3.

SUMMARY

1. Diantipyryl-o-nitrophenylmethane, diantipyryl-m-nitrophenylmethane, diantipyryl-p-nitrophenylmethane, diantipyryl-p-chlorophenylmethane, diantipyryl-α-naphthylmethane and diantipyryl-m-methoxy-p-hydroxyphenylmethane are leuco compounds of the corresponding dyes.

2. Introduction of a nitro group or chlorine into the molecule of diantipyryl-phenylcarbinol in the para-position to the central carbon atom lowers the dissociation of the hydroxyl group.

3. Hydrolysis of dyes containing antipyrine nuclei in 60% aqueous acetone is approximately 10 times as great as in water.

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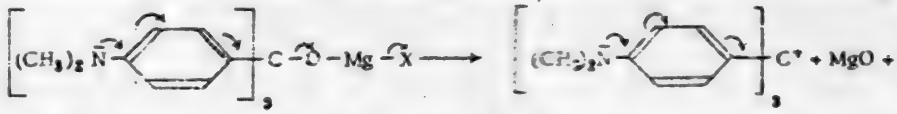
* See Consultants Bureau English translation, page 1575.

INTERACTION OF AMINOTRIARYLCARBINOLS WITH ORGANOMAGNESIUM COMPOUNDS

O. F. Ginzburg

It is known that magnesium alcoholates in the majority of cases do not undergo further transformations under the influence of organomagnesium compounds and the literature only mentions a few cases of reaction between magnesium alcoholates and organomagnesium compounds, leading ultimately to substitution of the alcoholate group OMgX by a hydrocarbon radical [1]. Bearing in mind that in aminotriphenylcarbinols the mobility of the hydroxyl groups is especially great and many times greater than the mobility of the hydroxyl groups in alcohols, it might be expected that also the O-magnesium derivatives of aminotriphenylcarbinols will readily decompose with rupture of the carbon-oxygen bond. Experiments confirmed this supposition. Thus, for example, on mixing phenetole solutions of 4,4',4"-hexamethyltriamino-triphenylcarbinol and methylmagnesium iodide, apart from evolution of methane, the formation is observed of a dye which partly remains in solution and imparts to the latter an intense color. Formation of a dye shows that decomposition occurs in the reaction mass of the magnesium derivative of 4,4',4"-hexamethyltriamino-triphenylcarbinol. This decomposition may be represented by the following scheme:



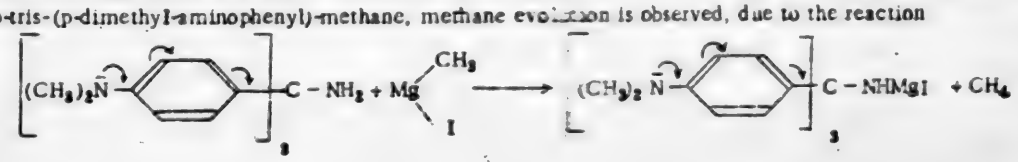
Similar results were obtained in a study of the reaction of 4,4'-tetramethyl-diamino-triphenylcarbinol, 9-phenyl-9-hydroxy-10-methyl-9,10-dihydroacridine, and diantipyryl-phenylcarbinol with methylmagnesium iodide.

As already shown by Freund and Beck [2], crystal violet enters into reaction with organomagnesium compounds with formation of derivatives of tetrasubstituted methane. Consequently, if 4,4',4"-hexamethyltriamino-triphenylcarbinol is treated with a few equivalents of methylmagnesium iodide, the initially formed dye enters into further reaction with the methylmagnesium iodide to give α,α,α-tris-(p-dimethylaminophenyl)-ethane.

Similarly, the reaction of 4,4'-tetramethyldiamino-triphenylcarbinol with methylmagnesium iodide gave α-phenyl-α,α-bis-(p-dimethylaminophenyl)-ethane. The preparation of α,α,α-tris-(p-dimethylaminophenyl)-ethane and of α-phenyl-α,α-bis-(p-dimethylaminophenyl)-ethane was performed by adding a solution of methylmagnesium iodide in ether to a benzene-ether solution of the respective aminotriphenylcarbinol. In this reaction it was noted that formation of the dye is hindered if the methylmagnesium iodide is added to the benzene-ethereal solutions of the aminotriphenylcarbinols in large portions. This is because organomagnesium compounds are capable of adding on to the amino groups of aminotriphenylcarbinols, thereby eliminating the influence of the amino groups on the polarization of the linkage between the methane carbon atom and the oxygen atom, and so hindering the rupture of this linkage.

It should be mentioned that neither α-phenyl-α,α-bis-(p-dimethylaminophenyl)-ethane nor α,α,α-tris-(p-dimethylaminophenyl)-ethane could be converted into a dye with the help of lead peroxide.

Further experiments showed that formation of dyes also occurs on interaction of organomagnesium compounds with amino bases of triphenylmethane dyes. To mention one example, in the action of methylmagnesium iodide on α-amino-tris-(p-dimethyl-aminophenyl)-methane, methane evolution is observed, due to the reaction



and there is also obtained crystal violet which, in presence of methylmagnesium iodide in the reaction mass, enters into reaction with the latter with formation of the above-mentioned α,α,α-tris-(p-dimethylaminophenyl)-ethane. But when methylmagnesium iodide acts on α-anilino-4,4'-bisdimethylaminotriphenylmethane at room temperature, as would be anticipated, no methane evolution is observed but malachite green is formed. The latter gradually enters into reaction with methylmagnesium iodide to form the above-noted α-phenyl-α,α-bis-(dimethylaminophenyl)-ethane.

Consequently, organomagnesium compounds, like strong acids, decompose amino bases and convert them into dyes.

EXPERIMENTAL

1. Determination of active hydrogen was carried out by the Chugaev-Tserevitinov method in phenetole solution at room temperature. The data obtained are set forth in the table.

No. of preparation	Name of substance	Wt. (g)	CH_4 (0°, 760 mm) (in ml) evolved in 20 min.	CH_4 (0°, 760 mm) (in ml) calculated	Color of reaction mass
1	4,4'-Tetramethyldiaminotriphenylcarbinol	0.1963	12.2	12.7	Green
		0.2010	12.1	13.0	
2	4,4',4"-Hexamethyltriaminotriphenylcarbinol	0.2142	10.4	12.3	Violet
		0.2149	10.6	12.4	
3	Diampyryl-phenylcarbinol	0.2561	11.5	12.0	Orange
		0.2137	9.2	10.0	
4	9-Phenyl-9-hydroxy-10-methyl-9,10-dihydroacridine	0.2653	18.0	20.6	Light-brown
		0.2581	17.4	20.2	
5	α-Amino-tris-(p-dimethylaminophenyl)-methane	0.2061	10.4	11.9	Violet
		0.2012	10.0	11.6	
6	α-Anilino-tris-(p-dimethylaminophenyl)-methane	0.2185	–	–	Violet
7	α-Anilino-4,4'-bis-dimethylaminotriphenylmethane	0.1913	–	–	Green

2. α-Anilino-tris-(p-dimethylaminophenyl)-methane. A mixture of 0.50 g of the methyl ether of 4,4',4"-hexamethyltriaminotriphenylcarbinol (m.p. 158°) and 0.60 g aniline is heated for 2 hours at 135-145°. The melt is cooled and dissolved in 15 ml ether and the solution cooled to 0°. A white crystalline precipitate soon appears and is filtered, well washed with ether and dried. Yield 0.30 g of substance with m.p. 189-190°.

0.1132 g substance: 11.8 ml N_2 (20°, 767); 0.1167 g substance: 12.2 ml N_2 (20°, 768). Found %: N 12.14, 12.19. $C_{31}H_{36}N_4$. Calculated %: N 12.05.

3. α-Phenyl-α,α-bis-(p-dimethylaminophenyl)-ethane. a) To a boiling solution of 2.42 g 4,4'-tetramethyldiamino-triphenylcarbinol in 60 ml ether-toluene (1 : 2) is slowly added from a dropping funnel, with stirring, an ethereal solution of methylmagnesium iodide prepared from 0.85 g Mg and 4.96 g methyl iodide. The first 10 ml of solution is run in in the course of 30 minutes. After standing for an hour, further addition of the ethereal solution of methylmagnesium iodide is effected dropwise at the rate of 20 ml solution in 2 hours. After again standing for an hour, the remaining 20 ml solution is introduced dropwise in the course of 40 minutes. The reaction mass is then stirred and heated for 12 hours. After decomposition of the reaction mass with ice, the ether-toluene solution is separated from the aqueous layer. The aqueous layer and also the obtained precipitate are treated twice with small portions of ether which are then added to the main ether-toluene solution. The latter is then treated with three portions of 100 ml each of 1% hydrochloric acid. To the resultant aqueous extracts is added a saturated solution of sodium acetate; the precipitate that forms is filtered after 4 hours, washed with water and dried at 80°. Yield 1.0 g with m.p. 128-131°. After 2 crystallizations from methyl alcohol the m.p. is 134°. A mixed sample with α-phenyl-α,α-bis-(p-dimethylaminophenyl)-ethane (m.p. 134°) melts at the same temperature.

b) To a boiling solution of 2.39 g α-anilino-4,4'-bis-dimethylamino-triphenyl-methane in 60 ml ether-toluene mixture (1 : 2) is slowly added 50 ml ethereal solution of methylmagnesium iodide prepared from 0.64 g Mg and 3.8 g methyl iodide. Synthesis is effected as described in 3 a). Yield 0.6 g with m.p. 132-133°. After

crystallization from alcohol the m.p. is 134°. A mixture of the prepared compound with α-phenyl-α,α-bis-(p-dimethylaminophenyl)-ethane (m.p. 134°) melts at the same temperature.

4. α,α,α-Tris-(p-dimethylaminophenyl)-ethane. To a boiling solution of 1.56 g 4,4',4"-hexamethyltriamino-triphenylcarbinol in 60 ml ether-toluene mixture (1 : 2) is slowly added 50 ml of an ethereal solution of the methylmagnesium iodide prepared from 0.59 Mg and 3.41 g methyl iodide. The synthesis is performed as described in 3 a). Yield 0.72 g substance with m.p. 201°. After crystallization from methyl alcohol the m.p. is 209-210°. Mixed test with α,α,α-tris-(p-dimethylaminophenyl)-ethane (m.p. 209-210°) gave the same melting point.

SUMMARY

In the interaction of aminotriarylcarbinols with organomagnesium compounds, apart from hydrocarbons, dyes are formed. The latter are also prepared by the action of organomagnesium compounds on the amino bases of triphenylmethane dyes.

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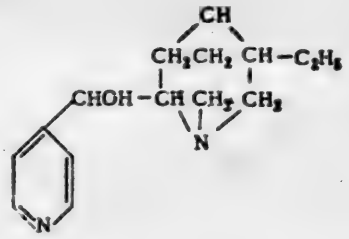
SYNTHESIS OF [5-ETHYLQUINUCLIDYL-(2)]-[PYRIDYL-(2)]-CARBINOL. V

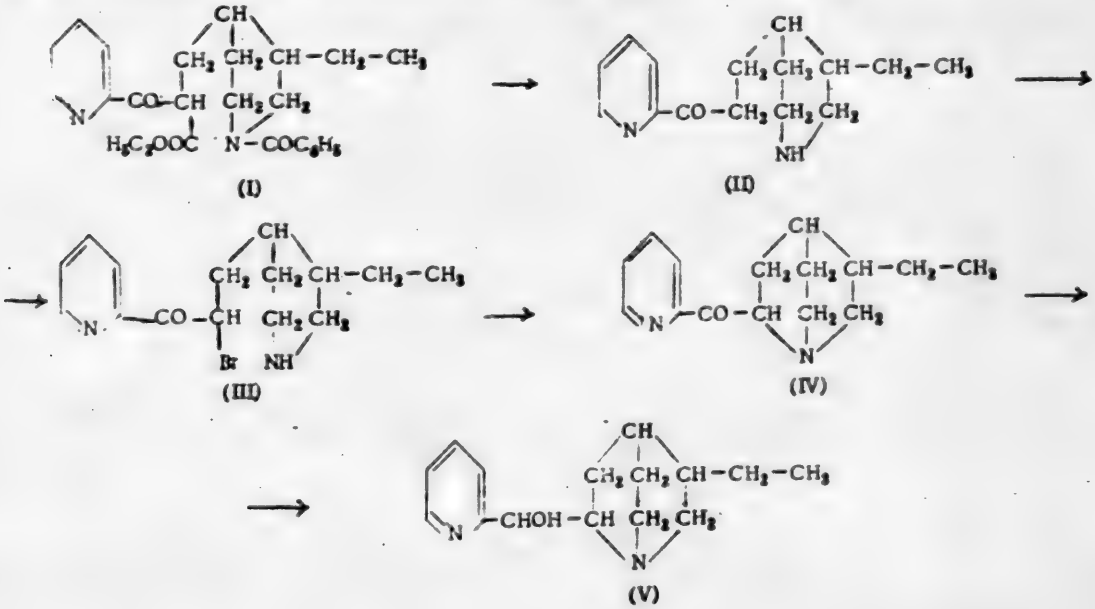
M. V. Rubtsov and V. A. Volskova

Comparison of hydroquinine with its pyridine analog containing a quinuclidine ring in the 4-position of the pyridine nucleus [1]



enabled us to establish that replacement of the quinoline nucleus in hydroquinine by a pyridine nucleus has relatively little effect on the chemotherapeutic activity of the preparation. It was interesting to ascertain the effect on the activity of the pyridine analog of hydroquinine of transfer of the ethylquinuclydyl-hydroxymethyl group from the 4-position to the 2-position of the pyridine nucleus.

For this purpose we synthesized [5-ethylquinuclidyl-(2)]-[pyridyl-(2)]-carbinol, starting from ethyl picolinate and ethyl benzoylhomocincholoiponate. Condensation of these esters gave the ketoesters (I) which was converted by acid saponification into {2-[3-ethylpiperidyl-(4)]-ethyl} -[pyridyl-(2)]-ketone (II).



Preparation of [5-ethylquinuclidyl-(2)]-[pyridyl-(2)]-ketone (IV) was carried out by the usual method via the corresponding C-bromo derivative (III).

Ethylquinuclidyl-pyridyl ketone (IV) is a light-yellow oil which distils in vacuum without decomposition; it exhibits the phenomenon of mutarotation. The carbonyl group of this compound is readily reduced to carbinol by hydrogenation of the dihydrochloride in an aqueous medium in presence of palladium black. The resultant mixture of stereoisomeric carbinols (V) is isolated in the form of a viscous oil which distilled in vacuum and, like hydroquinine, is transformed into the corresponding toxine (VI) by boiling with dilute acetic acid.

Attempts to resolve the stereoisomeric carbinols with the help of d-tartaric or d-camphorsulfonic acid were unsuccessful; the mixture of stereoisomers was therefore subjected to chemotherapeutic examination and found to be inactive in avian malaria.

The tests were carried out on siskins infected with Plasmodium relictum.

EXPERIMENTAL

{β-[3-Ethylpiperidyl-(4)]-ethyl}-[pyridyl-(2)]-ketone (II)

To sodium ethylate, prepared from 2.4 g metallic sodium powder and 4.8 g absolute alcohol, in an ethereal medium was added with stirring 15 g ethyl picolinate and 17 g ethyl N-benzoylhomocincholoiponate. The ether was removed by heating the reaction mixture to 80° (bath temperature) and the mass was stirred at this temperature for 4 hours. On cooling, the mass was mixed with 150 ml iced water. The unreacted starting materials were extracted with ether and the aqueous solution was made neutral to litmus with the help of 10% sulfuric acid. The oil which separated out was extracted with ether and the extract dried with anhydrous sodium sulfate. After driving off the ether, 12.47 g (56.1%) {β-[3-ethyl-N-benzoyl-piperidyl-(4)]-α-carbethoxyethyl}-[pyridyl-(2)]-ketone (ketoester) was obtained in the form of a viscous dark-red oil.

Without further purification, the obtained ketoester was subjected to ketonic cleavage by boiling for 4 hours with ten times the quantity of 17% hydrochloric acid. After cooling, the solution was washed with ether several times to remove benzoic acid and then made alkaline with excess of 50% potassium hydroxide. The resultant oil was extracted with ether and the extract dried with potassium carbonate. Removal of the ether left 5.88 g {β-[3-ethylpiperidyl-(4)]-ethyl}-[pyridyl-(2)]-ketone in the form of a viscous dark-yellow oil. For the purpose of purification the ketone was dissolved in 10 ml absolute alcohol, 1.05 g anhydrous oxalic acid in 5 ml absolute alcohol was added and the solution was diluted with 125 ml dry acetone. After a few minutes a copious crystalline precipitate had formed. After standing overnight, the precipitate was filtered, washed with acetone and ether and recrystallized from a small quantity of alcohol. Yield 3.92 g (44.6%). A white crystalline powder with m.p. 175.5-177°, readily soluble in water and alcohol, insoluble in acetone and ether.

2.739 mg substance: 6.626 mg CO_2, 1.950 mg H_2O. 4.709 mg substance: 0.308 ml N_2 (22.5°, 726.5 mm). Found %: C 65.97; H 7.96; N 9.34. $(C_{15}H_{22}ON_2)_2 \cdot C_2H_2O_4$. Calculated %: C 65.94; H 7.96; N 9.61.

The base, isolated from the oxalate, is a light-yellow oil, readily soluble in alcohol, ether, acetone and chloroform.

[5-Ethylquinuclidyl-(2)]-[pyridyl-(2)]-ketone (IV)

To a solution of 2.69 g {β-[3-ethylpiperidyl-(4)]-ethyl}-[pyridyl-(2)]-ketone in 19 ml 48% hydrogen bromide, heated to 60°, was added 1.74 g bromine in 9 ml 48% hydrogen bromide over a period of 15 minutes. When the addition was ended, the reaction mass was stirred for 20 minutes at 80°; the solution of the obtained bromoketone was then evaporated in a vacuum at 50°. The residue (6.72 g) was mixed with a solution of 12.2 g sodium bicarbonate in 60 ml water and 60 ml chloroform. The mixture was shaken for 2 hours, after which the chloroform layer was separated from the aqueous layer; the latter was extracted with chloroform and the extract combined with the main chloroform solution. After drying with potassium carbonate and driving off the chloroform, a brown oil remained which was distilled in vacuum (0.3 mm) to give 1.73 g light-yellow, viscous oil, boiling at 155-156°. Yield 65% of the theoretical.

The substance dissolves readily in alcohol, ether, acetone and chloroform, sparingly in water; it does not form crystalline salts with hydrochloric, oxalic and picric acids.

The freshly prepared solution in 96% alcohol has specific rotation $[\alpha]_D^{20}$ + 75.2°; after 24 hours, $[\alpha]_D^{20}$ + + 76.7° (c = 2.086; $\underline{l}$ = 1).

3.676 mg substance: 9.916 mg CO_2; 2.750 mg H_2O. 3.487 mg substance: 0.375 ml N_2 (31.5°, 728.5 mm). Found %: C 73.56; H 8.37; N 11.54. $C_{18}H_{22}ON_2$. Calculated %: C 73.72; H 8.25; N 11.47.

[5-Ethylquinuclidyl-(2)]-[pyridyl-(2)]-carbinol (V)

To a solution of 2.47 g [5-ethylquinuclidyl-(2)]-[pyridyl-(2)]-ketone in 20.2 ml 1 N hydrochloric acid was added 10 ml 2% palladium chloride solution. The mixture was shaken until the separated orange precipitate had dissolved; the solution was then hydrogenated at room temperature under a pressure of 40-60 mm water column. After the hydrogenation, the solution was filtered from catalyst and acidified with 40 ml 50% KOH. The base was extracted with ether and the extract dried with potassium carbonate. After driving off the ether, the residue was distilled in vacuum to give 2.38 g viscous oil which consisted of a mixture of the optical isomers of ethylquinuclidyl-pyridyl-carbinol. B.p. 139-143° at 0.3 mm. The oil had good solubility in alcohol, ether, chloroform; poor in water.

$[\alpha]_D^{20}$ + 70.8° in 96% alcohol (a 1.48; c 2.088; $\underline{l}$ = 1).

4.717 mg substance: 12.654 mg CO_2; 3.855 mg H_2O. 5.559 mg substance: 0.579 ml N_2 (24.5°, 723 mm). Found %: C 73.16; H 9.15; N 11.37. $C_{18}H_{22}ON_2$. Calculated %: C 73.12; H 9.01; N 11.37.

The prepared mixture must contain four stereoisomeric carbinols. Attempts to effect their resolution with the help of d-tartaric or d-camphorsulfonic acid proved unsuccessful. Boiling with dilute acetic acid leads to cleavage of the quinuclidine ring, this behavior being characteristic of the quinine alkaloids; in this case it led to formation of {β-[3-ethylpiperidyl-(4)]-ethyl}-[pyridyl(2)]-ketone.

SUMMARY

1. [5-Ethylquinuclidyl-(2)]-[pyridyl-(2)]-ketone was synthesized.

2. Catalytic hydrogenation of the ketone gives a mixture of the optical isomers of the corresponding carbinol which, on boiling with dilute acetic acid, undergoes like compounds of the quinine series, the reaction of "hydramino cleavage," and is transformed into {β-[3-ethylpiperidyl-(4)]-ethyl}-[pyridyl-(2)]-ketone.

3. The mixture of optical isomers of [5-ethylquinuclidyl-(2)]-[pyridyl-(2)]-carbinol proved to be inactive in tests on siskins infected with Plasmodium relictum.

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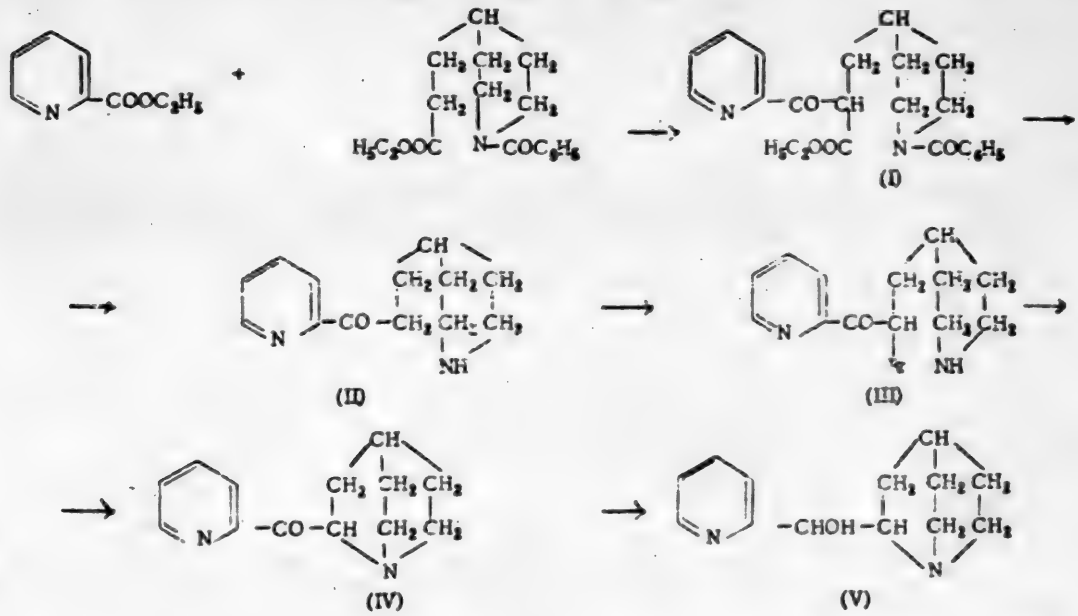
SYNTHESIS OF [QUINUCLIDYL-(2)]-[PYRIDYL-(2)]-CARBINOL. VI

M. V. Rubtsov and V. A. Volskova

In our previous papers we described analogs of hydroquinine containing the ethylquinuclidyl-carbonyl group in the 4- and 2-positions of the pyridine ring [1].

With the aim of further studying compounds of this series, we have synthesized [quinuclidyl-(2)]-[pyridyl-(2)]-carbinol. This compound was prepared from ethyl picolinate and ethyl β-[N-benzoylpiperidyl-(4)]-propionate.



The ketoester (I), prepared by condensation of the starting esters, was saponified with hydrochloric acid to {β-[piperidyl-(4)]-ethyl}-[pyridyl-(2)]-ketone (II), which was isolated in the form of the monohydrochloride melting at 182.5-184.5°. Treatment of the piperidylethyl-pyridyl-ketone with bromine in 48% hydrobromic acid gave the dihydrobromide of the corresponding C-bromoketone (III), a yellow crystalline powder with m.p. 170-171°. By treatment with bicarbonate solution, the bromoketone (III) was transformed into quinuclidyl-pyridyl-ketone (IV), which was obtained in the form of white prisms with m.p. 71.5-73°. Reduction of ketone (IV) to carbinol (V) was performed by hydrogenation of the dihydrochloride of the ketone in an aqueous medium in presence of palladium black. A mixture of the diastereoisomeric racemates was obtained in this way and was resolved by taking advantage of the differing solubility of their hydrochlorides in alcohol. The properties of the racemates are set forth in the table.

In tests on siskins infected with Plasmodium relictum, both racemates proved to be inactive.

EXPERIMENTAL

{β-[Piperidyl-(4)]-ethyl}-[pyridyl-(2)]-ketone (II)

To the sodium ethylate prepared from 1.25 g pulverized metallic sodium and 2.5 g absolute alcohol in a medium of absolute ether was added 7.5 g ethylpicolinate and 8.5 g ethyl β-[N-benzoyl-piperidyl-(4)]-propionate.

Designation of racemates	Base	Hydrochloride	Characteristic features
A	White clusters of needles, m.p. 118-119°	White microscopic prisms, m.p. 232-233°	Hydrochloride poorly soluble in cold alcohol
B	Small white prisms, m.p. 80-82°	White crystalline powder, m.p. 175-177°	Hydrochloride highly soluble in alcohol

The mixture was gradually heated on an oil bath to 80°; at the same time the ether was driven off. The mass was stirred for 4 hours at 80°, after which 50 ml benzene was added. The mixture was cooled to room temperature and shaken with 75 ml iced water. The aqueous layer was separated from the benzene layer, washed with ether, and treated with 10% sulfuric acid solution until neutral to litmus. The separated oil was extracted with ether and the extract dried with potassium carbonate. The ether was driven off to leave 5.91 g (57.6%) of {β-[N-benzoyl-piperidyl-(4)]-α-carbethoxyethyl}-[pyridyl-(2)]-ketone (ketoester).

The obtained ketoester was subjected to ketonic cleavage by boiling for 4 hours with ten times the quantity of 17% hydrochloric acid. After cooling, the solution was treated with 20% KOH until the reaction was weakly acid to Congo, washed with ether to remove benzoic acid and made alkaline with excess of 50% KOH. The separated base was extracted with ether and the extract dried with potassium carbonate. The ether was driven off and its last traces removed in vacuum to leave 2.23 g {β-[piperidyl-(4)]-ethyl}-[pyridyl-(2)]-ketone in the form of a light-brown oil. Yield 75.6% of theory.

The base was dissolved in 8 ml dry acetone and to the solution was added the calculated amount (for formation of monohydrochloride) of 14% alcoholic solution of HCl. The precipitate was filtered, washed with dry acetone and dried, giving 2.2 g of the hydrochloride with m.p. 182.5-184.5°.

The hydrochloride crystallizes from alcohol-acetone (1 : 1) in the form of white, prismatic plates melting at 189.5-190°. Good solubility in water, alcohol and chloroform; insoluble in ether.

3.146 mg substance: 7.058 mg CO_2; 2.070 mg H_2O. 4.302 mg substance: 9.654 mg CO_2, 2.990 mg H_2O. Found %: C 61.18, 61.20; H 7.36, 7.65. $C_{13}H_{16}ON_2 \cdot HCl$. Calculated %: C 61.27; H 7.52.

Dihydrobromide of {β-[Piperidyl-(4)]-α-bromoethyl}-[pyridyl-(2)]-ketone (III)

To a solution of 2 g monohydrochloride of {β-[piperidyl-(4)]-ethyl}-[pyridyl-(2)]-ketone in 7.5 ml 48% hydrogen bromide, heated to 50°, was added with stirring in the course of ten minutes, a solution of 1.25 g bromine in 9 ml 48% hydrogen bromide. The temperature was then raised to 80° and the stirring continued for another 15 minutes. The solution was evaporated in a vacuum at 55° until formation of a caramel-like mass. The latter went into solution when mixed with 1 ml absolute alcohol and the solution rapidly deposited a precipitate. Precipitation was completed by adding 25 ml dry acetone to the mixture. After brief standing, the precipitate was filtered, washed with dry acetone and then with ether, and dried in a vacuum-desiccator over sulfuric acid and potassium hydroxide.

A yellow, crystalline powder, m.p. 170-171° (with decomposition). Good solubility in water and alcohol, insoluble in acetone. Yield 3.08 g (84.6%).

0.1275 g substance: 0.1555 AgBr. Found %: Br 51.9. $C_{13}H_{17}ON_2Br \cdot 2HBr$. Calculated %: Br 52.3.

[Quinuclidyl-(2)]-[pyridyl-(2)]-ketone (IV)

To a mixture of 2.85 g {β-[piperidyl-(4)]-α-bromoethyl}-[pyridyl-(2)]-ketone and 40 ml chloroform was added a solution of 3.1 g sodium bicarbonate in 45 ml water. The mixture was shaken for 2 1/2 hours. The chloroform layer was then separated from the aqueous layer, dried with potassium carbonate and left to evaporate at room temperature. Evaporation of the chloroform left a dark-yellow, crystalline powder weighing 1.22 g, m.p. 62.5-67°. After recrystallization from gasoline (90-100° fraction), the substance was obtained in the form of white prisms melting at 71.5-73°. Good solubility in alcohol, acetone, chloroform, ether and hot gasoline. The analytical data agree with the composition [quinuclidyl-(2)]-[pyridyl-(2)]-ketone. Yield 0.71 g (53.7%).

4.477 mg substance: 11.819 mg CO_2; 2.904 mg H_2O. 3.712 mg substance: 9.841 mg CO_2; 2.428 mg H_2O. Found %: C 72.00, 72.30; H 7.25, 7.32. $C_{13}H_{16}ON_2$. Calculated %: C 72.18; H 7.46.

[Quinuclidyl-(2)]-[pyridyl-(2)]-carbinol (V)

A solution of 3.19 g quinuclidyl-pyridyl-ketone in 58.9 ml hydrochloric acid (0.1 N) was mixed with 10 ml 2% palladium chloride and subjected to hydrogenation under a pressure of 50-70 cm water column. At the end of the hydrogenation the catalyst was filtered off and the filtrate worked up with excess of 50% KOH. The separated base was extracted with ether and the extract dried with potassium carbonate. The ether was driven off to leave 3.15 g of a mixture of diastereoisomeric racemates of quinuclidyl-pyridyl-carbinol in the form of a crystal mass melting at 69-89°.

3.316 mg substance: 8.741 mg CO_2; 2.492 mg H_2O. 5.976 mg substance: 0.595 ml CH_4 (0°, 760 mm). Found %: C 71.88; H 8.41; OH 7.60. $C_{13}H_{18}O_2N_2$. Calculated %: C 71.51; H 8.31; OH 7.80.

The diastereoisomeric racemates were resolved by taking advantage of the differing solubilities of their hydrochlorides in alcohol.

3.08 g of the mixture of diastereoisomeric racemates of quinuclidyl-pyridyl-carbinol was dissolved in 14 ml absolute alcohol and to the solution was added the amount of 17% alcoholic hydrogen chloride calculated for formation of the monohydrochloride. The resultant precipitate was filtered from mother liquor (mother liquor 1) and washed with absolute alcohol and ether. Yield 1.42 g hydrochloride with m.p. 222.5-225°. After recrystallization from absolute alcohol the hydrochloride melted at 232-233°. White microscopic prisms, readily soluble in water and chloroform, fairly readily soluble in hot alcohol (1 : 16), poorly soluble in cold alcohol (approx. 1 : 80). Analysis of this substance identified it as quinuclidyl-pyridyl-carbinol hydrochloride (hydrochloride of racemate A).

3.558 mg substance: 8.042 mg CO_2; 2.731 mg H_2O. Found %: C 61.64; H 7.49. $C_{13}H_{18}ON_2 \cdot HCl$. Calculated %: C 61.27; H 7.52.

The base (racemate A) was isolated from the hydrochloride and melted at 118-119° after recrystallization from a gasoline fraction (70-90°). White clusters of needles with good solubility in water, alcohol, acetone and chloroform; poor in ether.

4.320 mg substance: 11.386 mg CO_2; 3.068 mg H_2O. Found %: C 71.73; H 8.31. $C_{13}H_{18}ON_2$. Calculated %: C 71.51; H 8.31.

Dihydrochloride: White crystals rapidly deliquescing in the air.

The alcoholic mother liquor from the hydrochloride (mother liquor 1) was evaporated in vacuum, the residue was dissolved in 7 ml absolute alcohol, and the solution diluted with 20 ml dry acetone. 1 g of a precipitate then came down; this was the hydrochloride of the second diastereoisomeric racemate (racemate B) contaminated with the hydrochloride of racemate A. The precipitate was filtered, washed with acetone; m.p. 175-185°. The mother liquor was evaporated in a vacuum, the residue was converted to the base with the help of 50% KOH solution, the base was extracted with ether and the extract dried with potassium carbonate. Removal of the ether left 0.38 g crystals with m.p. 73-79°. Two recrystallizations from gasoline (70-90° fraction) gave 0.26 g substance, as fine white prisms, melting at 80-82° (racemate B).

The substance has good solubility in water, alcohol, ether, chloroform and acetone, as well as in hot gasoline.

6.319 mg substance: 16.547 mg CO_2; 4.599 mg H_2O. 5.160 mg substance: 13.601 mg CO_2; 3.729 mg H_2O. Found %: C 71.42, 71.89; H 8.15, 8.08. $C_{13}H_{18}ON_2$. Calculated %: C 71.51; H 8.31.

Monohydrochloride: A white crystalline powder with m.p. 175-177°, readily soluble in water, alcohol and chloroform, poorly in acetone.

Boiling of the prepared racemates (A and B) with 50% acetic acid leads to cleavage of the quinuclidine ring, which process is characteristic of quinine alkaloids, and to conversion into {β-[piperidyl-(4)]-ethyl}-[pyridyl-(2)]-ketone.

SUMMARY

1. [Quinuclidyl-(2)]-[pyridyl-(2)]-ketone was synthesized.

2. Catalytic hydrogenation of this ketone gives a mixture of two diastereoisomeric racemates whose resolution was effected by exploiting the differing solubilities of their hydrochlorides in alcohol.

3. Boiling of the obtained racemates with 50% acetic acid resulted, as with other compounds of the quinine series, in the reaction of "hydraminic cleavage" and formation of {β-[piperidyl-(4)]-ethyl}-[pyridyl-(2)]-ketone.

Both racemates were found to be inactive in tests on siskins infected with Plasmodium relictum.

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•See Consultants Bureau Translation, page 1771.

IMIDAZOLE DERIVATIVES

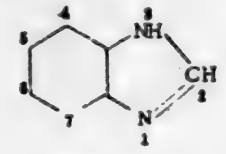
XL CONDENSATION OF PHTHALIC ANHYDRIDE WITH BENZIMIDAZOLE DERIVATIVES [1]

L. S. Efros, B. A. Porai-Koshits and S. G. Farbenshtein*

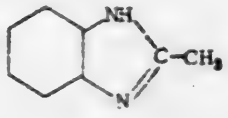
The valuable vat dyes include some derivatives of anthraquinone-containing imidazole rings [2]. They are usually obtained from diaminoanthraquinones whose synthesis is rather complicated. It, therefore, appeared expedient to attempt to prepare such compounds by another route, namely by condensing benzimidazole derivatives with phthalic anhydride. Such was the original purpose of this investigation.

It was found, however, that benzimidazole (I) itself is incapable of entering into condensation with phthalic anhydride. We know that substituents in the 5(6)-position have hardly any influence on the reactivity of benzimidazole [3]: we therefore decided to increase its activity by introducing substituents of the first order into the 2-position.

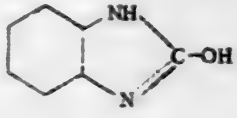
2- Methyl-benzimidazole (II) also proved incapable of condensation. On the other hand, 2-hydroxybenzimidazole (III) smoothly entered into this reaction and we obtained 5-o-carboxybenzoyl-2-hydroxybenzimidazole (IV), which is readily transformed by treatment with sulfuric acid into the anthraquinone derivative (V).



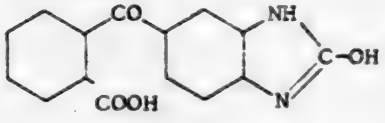
(I)



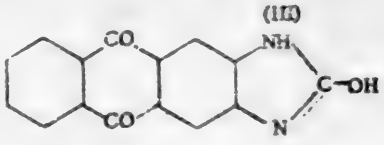
(II)



(III)



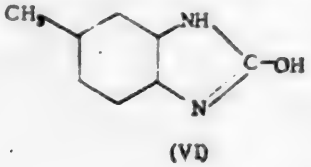
(IV)



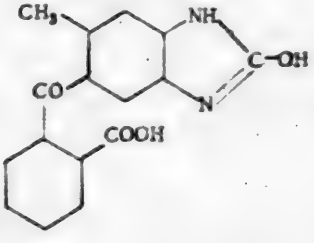
(V)

The structure of this product was confirmed by its synthesis from 2,3-diaminoanthraquinone and carbonyl chloride.

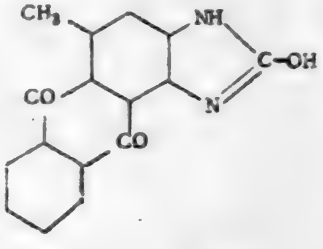
Equally successful was the performance of the reaction between phthalic anhydride and 5-methyl-2-hydroxybenzimidazole (VI), which gave the carboxylic acid (VII) and the anthraquinone derivative (VIII):



(VI)

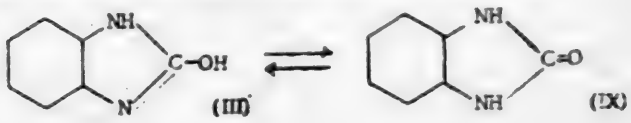


(VII)



(VIII)

As we know [4], 2-hydroxybenzimidazole (III) is tautomeric with o-phenyleneurea (IX)

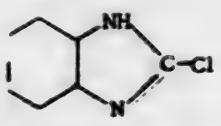


(III) (IX)

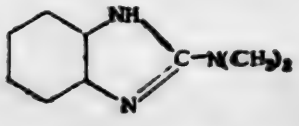
*Deceased

The very low basicity constant that we found in potentiometric titration of this substance [5] ($10^{-10.6}$) indicates that formula (IX) is more correct.

The question, therefore, arose as to which tautomeric form of this compound enters into the reaction under consideration. If it reacts in the form of o-phenyleneurea (IX), then only those benzimidazole derivatives which are susceptible to such a tautomerism should be capable of entering into the Friedel-Crafts reaction. We tested this point by synthesizing, starting from 2-chlorobenzimida zole (X), 2-dimethylaminobenzimidazole (XI) which is not susceptible to such transformations.

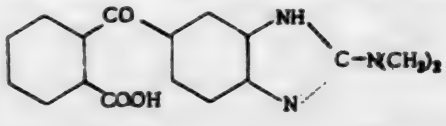


(X)

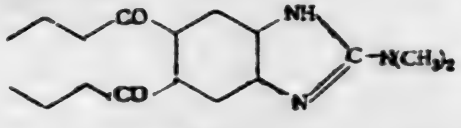


(XI)

It was found that this product smoothly enters into condensation with phthalic anhydride to form the carboxylic acid (XII) which undergoes transformation into the anthraquinone derivative (XIII)

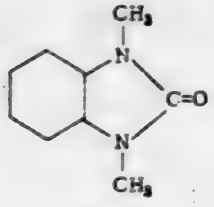


(XII)

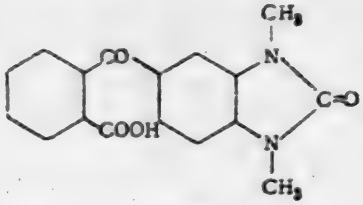


(XIII)

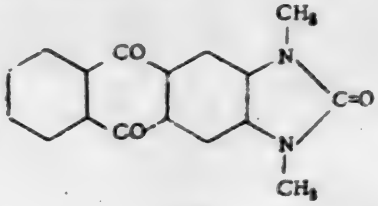
It was interesting to study also the reactivity of the o-phenyleneurea derivative (XI). The N,N-dimethyl derivative (XIV) required for this purpose is, as we established, readily obtained by direct methylation of 2-hydroxybenzimidazole with dimethylsulfate in presence of caustic alkali. The basicity constant of compound (XIV) was found to be of the same magnitude as that of the unmethylated product given above. This compound likewise readily reacted with phthalic anhydride to form the carboxylic acid (XV) and the anthraquinone derivative (XVI)



(XIV)



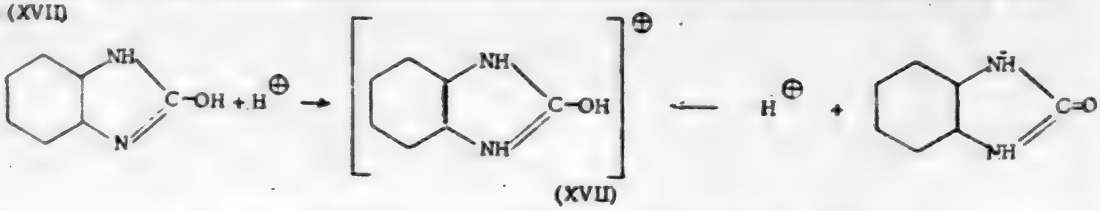
(XV)



(XVI)

Consequently, both of the tautomeric forms of 2-hydroxybenzimidazole are equ 'ly capable of smoothly condensing in the same direction with phthalic anhydride.

We explain this behavior by the fact that in the reaction conditions both tautomers form one and the same cation (XVII)



(XVII)

further reaction of which with phthalic anhydride leads to formation of the products described above.

Only those derivatives of benzimidazole which contain an active substituent of the first order in the 2-position are capable of entering into this reaction.

EXPERIMENTAL*

1. Starting Products

Benzimidazolone [6]. 24.6 g dry o-phenylenediamine hydrochloride is thoroughly triturated in a mortar with 10 g urea and the mixture is heated in a beaker on a paraffin wax bath to 150°. The mixture melts at first but after a short time it again solidifies. The melt is cooled, triturated in a mortar [illegible] in warm, dilute NaOH solution. The solution is filtered and hydrochloric acid is run into the [illegible] to benzimidazolone in the form of fine, faintly yellow leaflets. Yield of product 16 g (about 88%). [illegible]ly crystallizes from alcohol in the form of leaflets with m.p. 308°.

5-Methylbenzimidazolone [7]. Synthesis is performed as [illegible] om 20 g 3,4-toluenediamine and 20 g urea is obtained 16.5 g (70%) 5-methylbenzimidazol[illegible] tion from alcohol the m.p. is 292°.

1,3-Dimethylbenzimidazolone. 5 g benzimidazolone [illegible] OH and at 60° with intensive stirring addition is made dropwise to the solution of 7.[illegible] 25% alkali. A considerable amount of oil then rises to the surface of the mass [illegible] ght to the boil and refluxed for 1½ hours. The mass in the flask is then cooled [illegible] ing reaction product is filtered off. The precipitate is crystallized from 150 ml w[illegible] al. The resultant long, colorless needles contain water of crystallization. Yield 4[illegible] uum-desiccator, the product is crystallized from ligroine. Fine prisms with m.[illegible]

0.1443 g sub.: 21.8 ml N_2 (23°, 757 mm). Found %: [illegible] %: N 17.27.

2-Chlorobenzimidazole. 1.34 g benzimidazole, 6.7 ml [illegible] drops concentrated hydrochloric acid are heated in a sealed tube for 3 hours at 1[illegible] oxychloride is driven off from the resultant dark-brown solution in vacuum and the r[illegible] with ice water. The liquid is filtered from impurities and the filtrate neutralized w[illegible] of whitish needles of 2-chlorobenzimidazole is obtained from the weakly acid solution[illegible] by crystallization from aqueous alcohol. Lustrous, colorless leaflets with m.p. 212-215°. [illegible] g. The product is soluble in dilute inorganic acids and in solutions of caustic alkalies.

0.1015 g sub.: 15.9 ml N_2 (18°, 762 mm). 0.0969 g sub.: 0.0929 g AgCl. Found %: N 18.42; Cl 23.42. $C_7H_5N_2Cl$. Calculated %: N 18.37; Cl 23.28.

2-Dimethylaminobenzimidazole. 3 g 2-chlorobenzimidazole, 3.25 g dimethylamine hydrochloride and 2.24 g KOH in 30 ml water are heated in a sealed tube at 150-160° for 5-6 hours. A light-grey precipitate comes down after cooling of the reaction mass and is filtered, washed with water and crystallized from alcohol. Yield 2.6-2.7 g (80%). Colorless microscopic prisms with m.p. 314-316°.

0.0992 g sub.: 22.7 ml N_2 (23°, 758 mm). Found %: N 26.31. $C_9H_{11}N_3$. Calculated %: N 26.07.

The product is readily purified also in the form of the hydrochloride which comes down from solution in the form of lustrous needles with m.p. 291°.

0.1085 g sub.: 19.3 ml N_2 (16°, 760 mm). 0.1235 g sub.: 6.25 ml 0.1 N NaOH. Found %: N 21.01; Cl 17.97. $C_9H_{11}N_3 \cdot HCl$. Calculated %: N 21.25; Cl 17.98.

2. Preparation of Anthraquinone Derivatives

a) From benzimidazolone. 3 g pure benzimidazolone and 3.4 g sublimed phthalic anhydride are mixed with 50 ml tetrachloroethane in a round-bottomed flask fitted with reflux condenser, stirrer and thermometer; the phthalic anhydride dissolves and the benzimidazolone remains in the form of a suspension. 10 g anhydrous aluminium chloride is added in the cold and the mass is heated to 90° with stirring. The aluminium chloride gradually dissolves and the contents acquire a dark, reddish-violet color. With progressive heating the color of the solution becomes lighter and a dark resin forms on the sides. After 3½ hours, the evolution of hydrogen chloride abates and the mixture, acidified with hydrochloric acid, is poured into a flask. The tetrachloroethane is distilled in steam and the reaction product is filtered (IV). Weight 3.57 g. Repeated reprecipitations from the sodium carbonate solution with hydrochloric acid followed by washing gives a colorless product with m.p. about 300°, readily soluble in glacial acetic acid, less readily in alcohol, and insoluble in water.

0.2838 g sub.: 0.6545 g CO_2; 0.0975 g H_2O. 0.3608 g sub.: 31.2 ml N_2 (23°, 762 mm). Found %: C 62.94; H 3.84; N 9.89. $C_{11}H_6O_4N_2$. Calculated %: C 63.83 H 3.57; N 9.93.

* N. A. Zakharova and S. Lotareichik took part in the experimental work

Cyclization of the benzoylbenzoic acid derivative (IV) to the anthraquinone derivative (V) is effected by heating 8 g of the product in solution with 70 ml concentrated sulfuric acid for one hour on a boiling water bath. The solution is poured into 300 ml water and the yellow reaction product is filtered off. Yield nearly quantitative. The product is easily purified by converting it to the vat. It is purified for analysis by crystallizing from quinoline or pyridine. Bright-yellow needles with m.p. above 350°.

0.1368 g sub.: 0.3396 g CO_2; 0.0520 g H_2O. 0.1897 g sub.: 17.2 ml N_2 (22°, 762 mm). 0.1285 g sub.: 11.6 ml N_2 (22°, 760 mm). Found %: C 67.75; H 4.25; N 10.4, 10.35. $C_{16}H_8O_3N_2$. Calculated %: C 68.18; H 3.05, N 10.60.

b) From 5-methylbenzimidazolone. The condensation is performed exactly as in the preceding case. From 10 g 5-methylbenzimidazolone and 10 g phthalic anhydride is obtained 12.8 g of benzoylbenzoic acid derivative (64% of the theoretical). The product is purified by crystallization from acetic acid. M.p. 294°.

0.1031 g sub.: 8.9 ml N_2 (25°, 754 mm). Found %: N 9.71. $C_{16}H_{12}O_4N_2$. Calculated %: N 9.46.

Cyclization to the anthraquinone derivative (VIII) is performed in sulfuric acid. The yield is nearly quantitative. Purification by crystallization from quinoline. Fine yellow needles melting at above 350°.

0.643 g sub.: 0.1623 g CO_2; 0.0222 g H_2O. 0.0778 g sub.: 7.2 ml N_2 (24°, 760 mm). Found %: C 68.88; H 3.86; N 10.52. $C_{16}H_{10}O_3N_2$. Calculated %: C 69.06; H 3.62; N 10.07.

c) From 1,3-dimethylbenzimidazolone. Condensation of 3 g product with 3 g phthalic anhydride in similar conditions gives 3.8 g benzoylbenzoic acid derivative (XV), which crystallizes well from aqueous acetic acid in the form of fine, faintly yellow needles with m.p. 268°.

0.2691 g sub.: 23.7 ml N_2 (23°, 755 mm). Found %: N 9.28. $C_{17}H_{14}O_4N_2$. Calculated %: N 9.03.

Cyclization of the product (XV) to the anthraquinone derivative (XVI) is performed in sulfuric acid. The yield is nearly quantitative. Purification by crystallization from glacial acetic acid. Long, bright-yellow needles melting at above 350°.

0.1016 g sub.: 8.6 ml N_2 (22° 762 mm). Found %: N 9.67. $C_{17}H_{12}O_3N_2$. Calculated %: N 9.59.

d) From 2-dimethylaminobenzimidazole. Condensation of 3 g product with 3 g phthalic anhydride gives 3.5 g benzoylbenzoic acid derivative (XII). After driving off the tetrachloroethane, the hydrochloride of this product collects in the form of a resin on the walls of the flask. The liquid is poured off and the product is dissolved in 70 ml hot water; the base is precipitated by adding sodium acetate. The product is washed and reprecipitated from its solution in sodium carbonate with acetic acid. Fine needles with a faint orange-to-pink color.

Without further purification the substance is treated with concentrated sulfuric acid and converted into the anthraquinone derivative (XIII). On pouring the sulfuric acid solution into water, the bright-yellow sulfate comes down (being poorly soluble in cold water). The product is purified by crystallizing its hydrochloride from water. The fine yellow needles of this salt melt at above 360° in a capillary. The base (orange-yellow) is insoluble in organic solvents. On heating it dissolves in aqueous caustic alkalies and its salt comes down on cooling.

0.1289 g sub.: 14.6 ml N_2 (22°, 760 mm). 0.1252 g sub.: 13.8 ml N_2 (22°, 764 mm). Found %: N 13.09, 12.82. $C_{17}H_{13}O_3N_2 \cdot HCl$. Calculated %: N 12.82.

SUMMARY

Out of a number of derivatives of benzimidazole, only those containing an active substituent of the first order in the 2-position are capable of entering into condensation with phthalic anhydride in presence of aluminum chloride. Among such compounds are benzimidazolone, 1,3-dimethylbenzimidazolone and the 2-dimethylamino derivative. All these compounds apparently react in the form of the corresponding cations.

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•See Consultants Bureau Translation, page 725.

REACTIONS OF 6-QUINOLINECARBOXALDEHYDE

B. P. Lugovkin

The chemical properties of the quinoline aldehydes, due to the difficulty of synthesis, have been little studied.

Thanks, however, to the work of V. M. Rodionov and M. A. Berkengeim, published in 1944 [1], the synthesis of some aldehydes, including 6-quinoline carboxaldehyde today does not present any special difficulties.

They obtained the aldehyde in a yield of up to 60% by oxidation of 6-methylquinoline with selenium dioxide at 150-210°

G. A. Melentyeva and S. I. Kanevskaya [2] have recently studied the aldol condensation of 6-quinolinecarboxaldehyde with nitroalkanes (nitroethane and α-nitropropane) followed by catalytic reduction of quinolyl-6-nitroalklanes to quinolyl-6-alkanolamines, which were identified in the form of their dihydrochlorides.

In view of the definite interest in the study of quinoline derivatives, we have investigated a whole series of reactions of 6-quinolinecarboxaldehyde synthesized by the method of Rodionov and Berkengeim.

We oxidized the aldehyde with selenium dioxide and found that the product of oxidation is quinoline-6-carboxylic acid in a yield up to 64% of the theoretical. The reaction takes place very violently at above 240°.

By treating the aldehyde with concentrated aqueous KOH (Cannizzaro reaction) we effected the previously unreported synthesis of 6-quinolyl alcohol in the form of colorless crystals with m.p. 81-82°, in a yield of 74% of the theoretical. Quinoline-6-carboxylic acid was isolated in a yield of up to 94% of the theoretical.

Heating of 6-quinolyl alcohol with methyl iodide, ethyl bromide and ethyl iodide led to the corresponding alkyl halides of the alcohol.

Resinous products were formed when an attempt was made to carry out the acyloin condensation of 6-quinolinecarboxaldehyde with potassium cyanide: 6,6'-quinoloin was extracted in insignificant amount (up to 5%) in the form of colorless crystals* with m.p. 167°. It is reported in the literature that some aromatic aldehydes such as, for example, amino- and nitrobenzaldehydes, do not give the corresponding benzoins [3].

We also condensed 6-quinolinecarboxaldehyde with primary aromatic amines. The Schiff bases of 6-quinolideneaniline and o-toluidine are described in the literature [4].

By heating the aldehyde with α-aminopyridine in alcoholic solution, we synthesized 6-quinolidene-α-aminopyridine in the form of colorless crystals with m.p. 139-140° in a yield of 86.4% of the theoretical. Heating with methyl iodide and ethyl iodide led to the corresponding dialkyl iodides.

Reaction of the aldehyde with β-naphthylamine gave 6-quinolidene-β-naphthylamine in the form of colorless crystals with m.p. 140-141°, in a yield of 90% of the theoretical. Its methiodide and ethiodide were synthesized.

Reaction with α-naphthylamine gave 6-quinolidene-α-naphthylamine in the form of an oily liquid in a yield of 83% of the theoretical. It was characterized as the picrate with m.p. 195-196°.

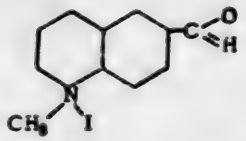
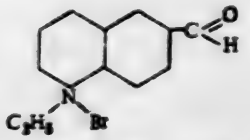
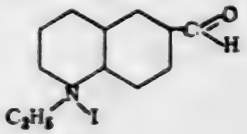
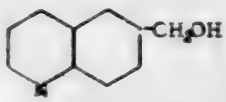
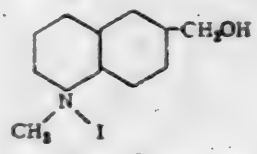
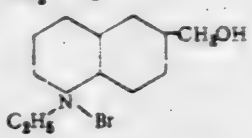
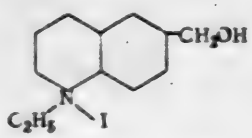
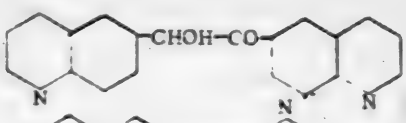
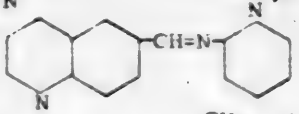
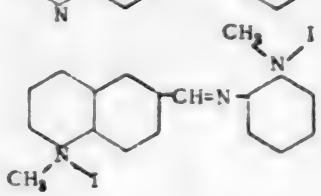
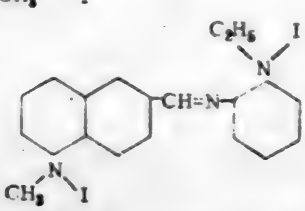
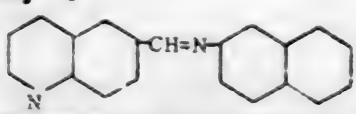
Reaction of the aldehyde (2 moles) with o-phenylenediamine gave 6,6'-diquinolidene-o-phenylenediamine in the form of pale-green crystals with m.p. 221-222°; yield 38% of the theoretical.

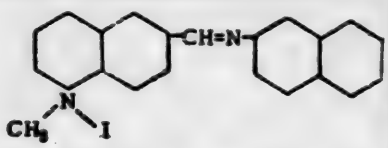
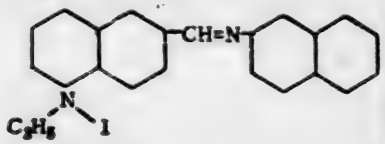
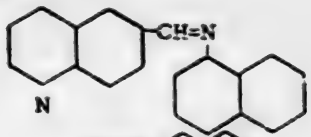
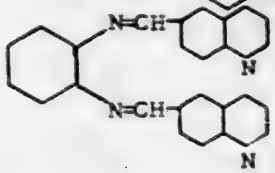
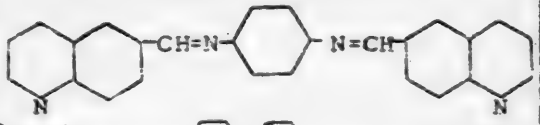
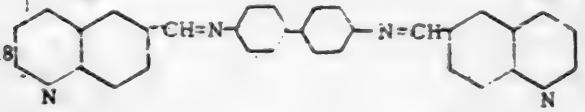
Reaction of the aldehyde (2 moles) with p-phenylenediamine gave 6,6'-diquinolidene-p-phenylenediamine in the form of light-green crystals with m.p. 252-253°, in a yield of 92% of the theoretical.

The product of reaction of 6-quinolinecarboxaldehyde (2 moles) with benzidine was 6,6'-diquinolidene-benzidine; yellow crystals with m.p. 262-264°; yield 84% of theory.

The constants of the synthesized 6-substituted quinolines are set forth in the table.

*After thorough purification, benzoin is colorless [3].

No. of Prep.	Formula	Melting point (°C)	Yield (in %)	Remarks
1		222	66	Literature, m.p. 218°
2		191-192	64	
3		195-196	80	
4		81-82	74	Picrate, m.p. 201-202°
5		170	66	
6		177-178	95	
7		132	91	
8		166-167	5	Picrate, m.p. 237-238°
9		139-140	86	
10		126-128	81	
11		119-120	53.6	
12		140-141	90	

No. of Prep.	Formula	Melting point (°C)	Yield (in %)	Remarks
13		210-214	86	
14		183-185	52	
15		Oily liquid	84	Picrate, m.p. 195-196°
16		221-222	38	
17		252-253	92	
18		262-264	84	

EXPERIMENTAL

In all the experiments anhydrous 6-quinolinecarboxaldehyde (m.p. 74-76°) was used; it is soluble in water, alcohol, ether dioxane, benzene and acetic acid. The picrate is prepared in alcoholic solution; after recrystallization from glacial acetic acid it forms dark-yellow crystals with m.p. 196-197°.

Action of Alkyl Halides on 6-Quinolinecarboxaldehyde

0.5 g aldehyde and 0.8 g methyl iodide were heated on a water bath at 85-90° for 30 minutes. After evaporating off the methyl iodide, the 6-quinolinecarboxaldehyde methiodide was repeatedly washed with absolute alcohol and dry ether; yield 0.62 g (65.9%) of yellow crystals with m.p. 222° [4]. The crystals readily dissolve in water, insoluble in ether and sparingly soluble in absolute alcohol.

0.0966 g sub.: 0.0758 g AgI. Found %: I 42.42. $C_{11}H_{10}ONI$. Calculated %: I 42.45.

0.8 g aldehyde and 1 ml ethyl bromide were heated in a sealed tube at 100-110° for 3 hours. After evaporating off the ethyl bromide, the ethobromide was repeatedly washed with dioxane while heating. Yield 0.87 g (64.0%) of pinkish crystals with m.p. 191-192°; no change in m.p. after repeated washing. Easily soluble in water, alcohol, glacial acetic acid; sparingly in dioxane.

0.0958 g sub.: AgBr 0.0670 g. Found %: Br 29.76. $C_{12}H_{12}ONBr$. Calculated %: Br 30.04.

0.5 g aldehyde and 0.8 g ethyl iodide were heated on a boiling water bath for 30 minutes. After evaporating the ethyl iodide, the ethiodide of the aldehyde was repeatedly washed with benzene and dry ether with heating. Yield 0.8 g (83%) dark-yellow crystals with m.p. 195-196°. Readily soluble in absolute alcohol and water; insoluble in benzene, dioxane, and dry ether.

0.1032 g sub.: 0.0776 g AgI. Found %: I 40.65. $C_{12}H_{12}ONI$. Calculated %: I 40.55.

Oxidation of 6-Quinolinecarboxaldehyde with Selenium Dioxide

5 g aldehyde and 2.5 g selenium dioxide (ground to powder) were mixed and heated in Wood's alloy; at 240° a very violent reaction commenced and the temperature rose to above 300°. After cooling, the mass was washed with water; lengthy extraction with alcohol led to isolation of 3.5 g (63.8%) quinoline-6-carboxylic acid with m.p. 278-280°. The acid was dissolved in an aqueous solution of potassium carbonate and boiled with active carbon; appropriate working-up gave colorless crystals with m.p. 290°. The literature [5] gives m.p. 290-292°. The picrate is prepared in alcoholic solution and forms small yellow needles with m.p. 239-240°; after recrystallization from glacial acetic acid the m.p. is 240-241°.

Action of Alkyl Halides on 6-Quinolinecarboxylic Acid

1 g acid and 5 ml ethyl bromide were heated in a sealed tube for 10 hours at 100°. After evaporation of the ethyl bromide, the original acid was obtained with m.p. 284-286°; mixed melting point 288°.

Heating of the acid (1 g) in the same conditions with ethyl iodide (2 ml) also gave the original acid: m.p. 288°.

Action of Aqueous KOH Solution on 6-Quinolinecarboxaldehyde

To 20 g aldehyde was added an aqueous solution of KOH (16 g KOH in 12 ml water). With thorough stirring thetemperature was raised from 20 to 75°; on cooling the temperature gradually fell to room temperature. After 6 hours the product was filtered in vacuum. The solid product was extracted with ether in an extractor until the 6-quinolyl alcohol was completely extracted (the filtrate was worked up with ether and the ethereal solution added to the main ethereal extract; the alkaline solution was treated for extraction of the acid). After driving off the ether, the residue, in form of orange, lustrous plates, was washed with water until neutral. Yield 8.8 g 6-quinolyl alcohol with a broad melting range (up to 77°). Fractional recrystallization from dioxane gave 7.5 g (74.1%) of pale-yellow crystals with m.p. 81°. Recrystallization from alcohol in presence of active carbon gave colorless crystals with m.p. 81-82°. The picrate forms yellow crystals with m.p. 201-202° (from alcohol).

From the solid residue (after extraction of the alcohol), dissolved in water, and from the alkaline filtrate was isolated 10.3 g (93.6%) of 6-quinolinecarboxylic acid by careful neutralization with hydrochloric acid (phenolphthalein and methyl orange). M.p. 287-288°. The acid was dissolved in aqueous potassium carbonate, boiled with active carbon and worked up to 6-quinolinecarboxylic acid in the form of a colorless powder with m.p. 290°. The picrate melted at 240-241°.

Analysis of the alcohol (Kjeldahl*): 0.4542 g sub.: 24.6 ml NaOH (T 1.0964). Found %: N 8.32. $C_{10}H_9ON$. Calculated %: N 8.81.

Action of Alkyl Halides on 6-Quinolyl Alcohol

0.5 g alcohol and 0.75 g methyl iodide were heated on a boiling water bath for 2 hours. The methyl iodide was driven off and the 6-quinolyl alcohol methiodide was repeatedly washed with dry ether. Yield 0.62 g (66%) yellow crystals with m.p. 164-166°. After recrystallization from alcohol, m.p. 170°; readily soluble in water, very sparingly in dioxane and dry ether.

0.0912 g sub.: 0.0708 g AgI. Found %: I 41.97. $C_{11}H_{12}ONI$. Calculated %: I 42.16.

0.5 g alcohol and 1 ml ethyl bromide were heated in a sealed tube at 90° for 3 hours. After driving off the ethyl bromide, the ethobromide of the alcohol was repeatedly washed with dry ether. Yield 0.8 g (95.2%) of rather dirty crystals with m.p. 166-170°. Recrystallization from dioxane and alcohol (a little) gave light-orange crystals with m.p. 177-178°. Readily soluble in water and alcohol, insoluble in dioxane and dry ether.

0.0965 g sub.: 0.0678 g AgBr. Found %: Br 29.90. $C_{12}H_{14}ONBr$. Calculated %: Br 29.62.

0.5 g alcohol and 1 g ethyl iodide were heated on a boiling water bath for 2 hours. After driving off the ethyl iodide, the ethiodide of the alcohol was repeatedly washed with dry ether. Yield 0.9 g (91%) yellow crystals with m.p. 120-131°. Recrystallization from dioxane and alcohol (in small amount) gave m.p. 132°. Readily soluble in alcohol and water; insoluble in dry ether and dioxane.

0.1122 g sub.: 0.0843 g AgI. Found %: I 40.61. $C_{11}H_{14}ONI$. Calculated %: I 40.29.

* Metallic mercury was added after heating for several days; during the distillation of the ammonia, zinc dust was added [H. Meyer, Determination of structure of organic compounds. State Sci.-Tech. Press, 129 (1935)].

The Acyloin Reaction

Expt. I. To 12 g 6-quinolinecarboxaldehyde, dissolved in 25 ml alcohol, was added 2.5 g potassium cyanide in 3 ml water. The solution became dark-brown after heating for 30 minutes on the boiling water bath. On pouring into water (200 ml) a resinous, dark-orange precipitate came down; the precipitate was filtered, treated several times with water at the boil (in this treatment an insignificant amount of unchanged 6-quinolinecarboxaldehyde came down from the aqueous solution), dissolved in alcohol and repeatedly digested with active carbon.

Removal of the ethanol left 1 g (8.3%) dark-yellow crystals with m.p. 157-159°. Two recrystallizations from alcohol gave colorless crystals with m.p. 166-167°; yield 0.6 g (50%). The picrate forms light-yellow crystals with m.p. 237-238° (from alcohol).

Expt. II. To 10 g aldehyde, dissolved in 50 ml alcohol, was added 2.5 g potassium cyanide in 3 ml water. Heating was carried out for an hour on the boiling water bath; subsequent treatment gave similar results.

0.1134 g sub.: 6.40 ml NaOH (T 1.0964). Found %: N 8.67. $C_{20}H_{12}O_2N_2$. Calculated %: N 8.92.

Action of α-Aminopyridine on 6-Quinolinecarboxaldehyde

3.9 g aldehyde and 2.4 g α-aminopyridine were heated in alcoholic solution (10 ml) at the boil (on a water bath) for 2 hours. Fractional recrystallization from alcohol (while evaporating) gave 5 g (86.4%) 6-quinolidene-α-aminopyridine in the form of colorless crystals with m.p. 138-139°. After a second recrystallization the m.p. was 139-140°. Sparingly soluble in benzene and water, readily in alcohol, glacial acetic acid and dioxane.

0.1572 g sub.: 18.75 ml NaOH (T 1.0964). Found %: N 18.32. $C_{15}H_{11}N_3$. Calculated %: N 18.03.

Action of Alkyl Halides on 6-Quinolidene-α-aminopyridine

1 g substance and 3.2 g methyl iodide were heated on a boiling water bath for 3 hours. After evaporation of the methyl iodide, the dimethiodide of 6-quinolidene-α-aminopyridine was repeatedly washed with dioxane while heating. Yield 1.8 g (81.1%) of light-yellow crystals with indefinite m.p. 119-120°. On recrystallization from glacial acetic acid, m.p. 126-128° (sintering at 136-139°). Readily soluble in water and alcohol, sparingly in dioxane.

0.0898 g sub.: 0.0818 g AgI. Found %: I 49.24. $C_{17}H_{17}N_3I_2$. Calculated %: I 49.10.

0.6 g substance and 3.3 g of ethyl iodide were heated on a boiling water bath for 2 hours. After evaporation of the ethyl iodide, the diethiodide of 6-quinolidene-α-aminopyridine was repeatedly washed with dioxane while heating. Yield 0.75 g (53.6%) of dark-yellow crystals with m.p. 119-120° (sintering at 122-124°). Soluble in water and alcohol, sparingly soluble in dioxane.

0.0960 g sub.: 0.0828 g AgI. Found %: I 46.63. $C_{19}H_{21}N_3I_2$. Calculated %: I 46.57.

Action of β-Naphthylamine on 6-Quinolinecarboxaldehyde

3 g aldehyde and 2.7 g β-naphthylamine were heated in alcoholic solution (10 ml) at the boil on a water bath for 2 hours. Crystals came down after cooling. Yield 4.75 g 6-quinolidene-β-naphthylamine. From the mother liquor was isolated a further 0.1 g of substance in the form of lustrous plates with m.p. 140-141°. The m.p. did not change after recrystallization. Soluble in alcohol and dioxane, insoluble in water.

0.4854 g sub.: 29.9 ml NaOH (T 1.0964). Found %: N 9.46. $C_{20}H_{14}N_2$. Calculated %: N 9.93.

Action of Alkyl Halides on 6-Quinolidene-β-naphthylamine

0.55 g substance and 1.8 g methyl iodide were heated in a sealed tube at 100° for 2 hours. After evaporation of the methyl iodide, the methiodide of 6-quinolidene-β-naphthylamine was repeatedly washed with dioxane with heating. Yield 0.7 g (65.3%) of dark-yellow crystals with m.p. 210-214° (with sintering). Soluble in alcohol, insoluble in water and dioxane.

0.0802 g sub.: 0.0445 g AgI. Found %: I 30.00. $C_{21}H_{17}N_2I$. Calculated %: I 29.93.

1 g substance and 3 g ethyl iodide were heated on a boiling water bath for 3 hours. After evaporation of the ethyl iodide, the ethiodide of 6-quinolidene-β-naphthylamine was repeatedly washed with dioxane with heating. Yield 0.8 g (51.6%) dark-yellow crystals with m.p. 183-185°, soluble in alcohol, insoluble in water and dioxane.

Action of α-Naphthylamine on 6-Quinolinecarboxaldehyde

3 g aldehyde and 2.7 g α-naphthylamine were heated on a boiling water bath for an hour. An oily liquid was formed with a small content of crystalline material which was filtered off after cooling. Yield 4.5 g (83.5%) 6-

quinolidene-α-naphthylamine.

The same results were obtained in an experiment with heating in alcohol for 2 hours.

To 1.7 g of the aldehyde in 3 ml ethanol was added an alcoholic solution (1.5 mole in 15 ml alcohol) of picric acid; a dark-yellow picrate came down with m.p. 194-195° (from 170° the picrate was green); yield 2.2 g (73.9%). Recrystallization from glacial acetic acid gave fine, golden-yellow needles with m.p. 195-196°.

0.2792 g sub.: 25.70 ml NaOH (T 1.0964).*

Found %: N 14.14. $C_{20}H_{14}N_2 \cdot C_6H_3O_7N_3$ Calculated %: N 13.80.

Action of o-Phenylenediamine on 6-Quinolinecarboxaldehyde

3 g aldehyde (2 moles) and 1 g o-phenylenediamine were heated in alcoholic solution (10 ml) at the boil on a water bath for an hour; after evaporation of the alcohol a crystalline and resinous product were isolated. 5 ml ethanol was added and the crystals were filtered off and washed with alcohol. Yield 1.4 g (37.9%) of di-6,6'-quinolidene-o-phenylenediamine in the form of light-green crystals with m.p. 216-217°. After recrystallization from alcohol, m.p. 221-222°. Crystals badly contaminated with resinous liquid were isolated from the mother liquor after evaporation of the ethanol; no more base could be extracted.

0.3898 g sub.: 38.00 ml NaOH (T 1.0964). Found %: N 14.98. $C_{26}H_{18}N_4$ Calculated %: N 14.51.

Action of p-Phenylenediamine on 6-Quinolinecarboxaldehyde

3 g aldehyde (2 moles) and 1 g p-phenylenediamine were heated in alcoholic solution (20 ml) at the boil for 2 hours; a finely crystalline, yellow product came down. After cooling, the product was filtered and washed with ethanol. Yield 3.4 g (92.1%) of di-6,6'-quinolidene-p-phenylenediamine in the form of light-yellow crystals with m.p. 241-242° (heating from 150° on a metal block). After recrystallization from glacial acetic acid the m.p. was 252-253° (with preliminary contraction). Very sparingly soluble in ethanol and dioxane, soluble in glacial acetic acid.

0.1828 g sub.: 17.10 ml NaOH (T 1.0964). Found %: N 14.37. $C_{26}H_{18}N_4$ Calculated %: N 14.51.

Action of Benzidine on 6-Quinolinecarboxaldehyde

3 g aldehyde and 1.76 g benzidine were heated in alcoholic solution (20 ml) at the boil for 2 hours; a yellow, finely crystalline precipitate was formed. After cooling, the precipitate was filtered and washed with ethanol. Yield 3.7 g (83.9%) di-6,6'-quinolidene-benzidine in the form of yellow, fine crystals with an indefinite melting point. After repeated washings with dioxane (while hot) and recrystallization from glacial acetic acid, the m.p. was 262-264° (heated on metal block from 150°) with preliminary contraction. Very sparingly soluble in alcohol and dioxane, soluble in glacial acetic acid.

0.1834 g sub.: 14.16 ml NaOH (T 1.0964). Found %: N 11.86. $C_{32}H_{22}N_4$ Calculated %: N 12.12.

SUMMARY

1. Reaction of ethyl bromide and ethyl iodide with 6-quinolinecarboxaldehyde gave the corresponding alkyl halide compounds.

2. Oxidation of 6-quinolinecarboxaldehyde with selenium dioxide leads to a very violent reaction with formation of quinoline-6-carboxylic acid.

3. 6-Quinolyl alcohol and 6-quinolinecarboxylic acid were synthesized by the action of concentrated aqueous solution of potassium hydroxide on 6-quinolinecarboxaldehyde. Treatment of the alcohol with methyl iodide, ethyl bromide and ethyl iodide gave the corresponding alkyl halide compounds.

4. The acyloin reaction of 6-quinolinecarboxaldehyde results in much resinification; 6,6'-quinoloin is isolated in insignificant amount.

5. 6-Quinolinecarboxaldehyde was condensed with α-aminopyridine, α- and β-naphthylamines, o- and p-phenylene diamines and benzidine. The corresponding 6-quinolidene-amines and 6,6'-diquinolidene-amines were synthesized.

*With preliminary reduction with zinc dust in concentrated H_2SO_4.

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[3] C. Weygand, Experimental Methods in Organic Chemistry, Vol. II, Foreign Literature Press, 371-372 (1950).

[4] Howitz, Philipp, Ann., 396, 31 (1913).

[5] Beilst., XXII, 79 (1935).

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Central Council of Trade Unions,
Chemical Laboratory

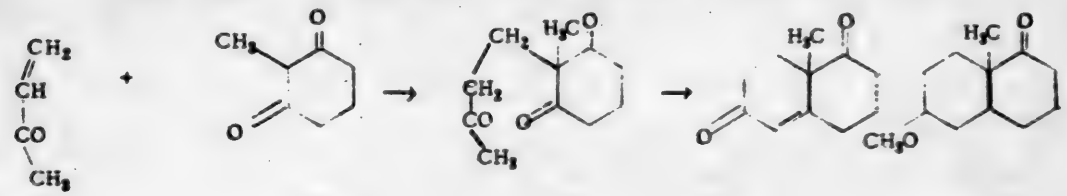
*See Consultants Bureau Translation, page 325.

SYNTHESIS OF STEROID COMPOUNDS AND RELATED SUBSTANCES

XXVII. CONDENSATION OF CYCLIC β-DIKETONES WITH VINYL KETONES AND TRANSFORMATIONS OF THE PRODUCTS OF THIS CONDENSATION. II

I. N. Nazarov and S. I. Zavyalov

We recently showed [1] that condensation of methylvinyl ketone (I) with methyldihydroresorcinol (II) gives the triketone (III), cyclization of which leads to 9-methyl-1,6-dikeio-$\Delta^{9(10)}$-octalin (IV)

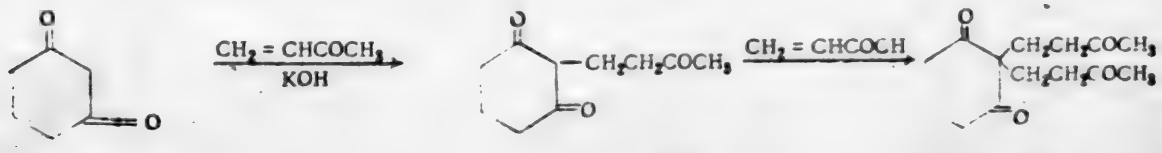


(I) (II) (III) (IV) (V)

The methoxyoctalone (V), similar in structure, has been successfully used in our laboratory for the preparation of steroid compounds of the cis-cis series by the method of diene condensations [2]. The diketooctalin (IV) may present great interest as a starting material for the synthesis of steroid hormones possessing a double bond in the C_4-C_5 position. Whereas the diketooctalin (IV) itself paves the way to synthesis of steroid molecules starting from ring A–B, by suitable choice of vinyl ketone and cyclic β-diketone we can construct a steroid system starting from ring C–D. For this purpose it is necessary to synthesize derivatives of diketodecalin (or 1,5-diketohydrindane) which would have in the 5- (or 4-) position a labile hydrogen or a substituent permitting the attachment of the remaining portion of the steroid molecule to the existing C–D ring system.

Our present investigation is also devoted to the possibility of synthesizing the bicyclic compounds in question by condensation of vinyl ketones with cyclic β-diketones.

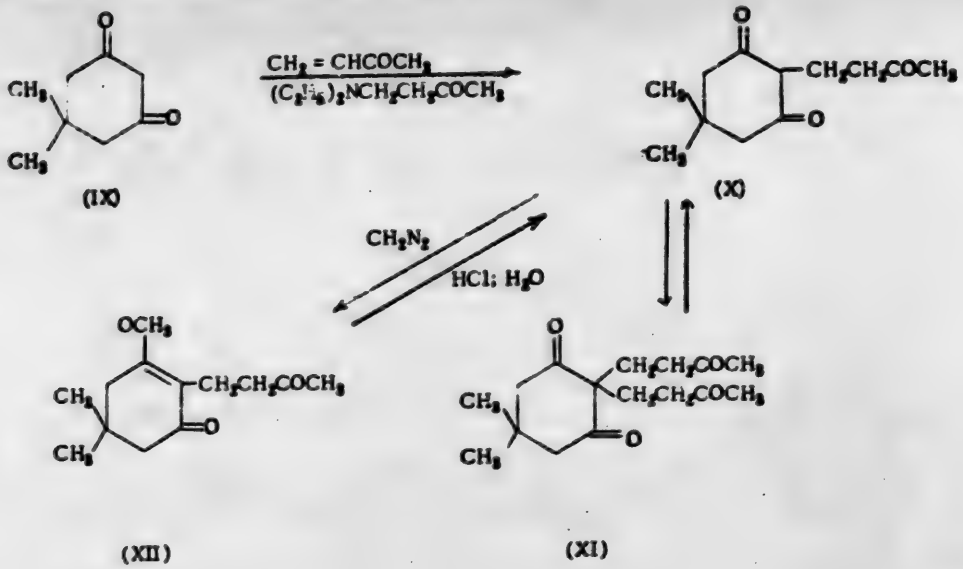
The reaction of methylvinyl ketone with dihydroresorcinol (VI) proceeds smoothly in methanol solution in presence of KOH, but a mixture of approximately equal amounts of the mono- and bis-adducts (VII) and (VIII) is then formed. The mono-adduct (VII) is a high-boiling liquid with strongly marked acidic properties, changing into the bis-adduct (VIII) under the action of methylvinyl ketone. Unlike the methyl derivative (III), which is smoothly converted into the bicyclic compound (IV), (γ-ketobutyl)-dihydroresorcinol (VII) proved to be fairly stable toward cyclizing agents. In presence of sodium alcoholate, phosphorus pentoxide or acetic anhydride, depending upon the temperatures, the substance either does not undergo any change or resinifies.



(VI) (VII) (VIII)

Interaction of methylvinyl ketone with dimedon (IX) also gives a mixture of mono- and bis-adducts (X, XI); the conversion of the first into the second compound is reversible; in presence of aqueous potassium carbonate

solution at 80-100° the bis-edduct is reconverted into the monoketobutyl derivative (X).



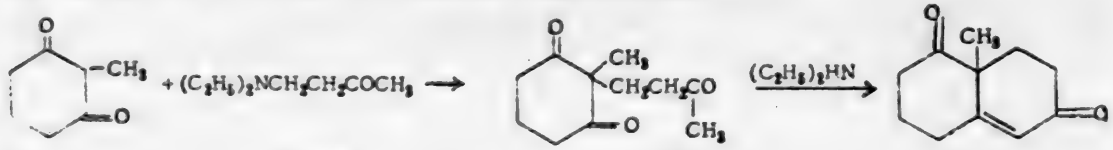
(IX) (X) (XII) (XI)

It is interesting to note that the corresponding bis-adduct of dihydroresorcinol does not split off methylvinyl ketone in the specified conditions.

The products of condensation of methylvinyl ketone with dimedon (X) and its enolic methyl ether (XII) do not give bicyclic compounds under the action of sodium alcoholate or phosphorus pentoxide. As in the case of the dihydroresorcinol derivative (VII), these compounds are either recovered unchanged from the reaction mixture or undergo considerable resinification.

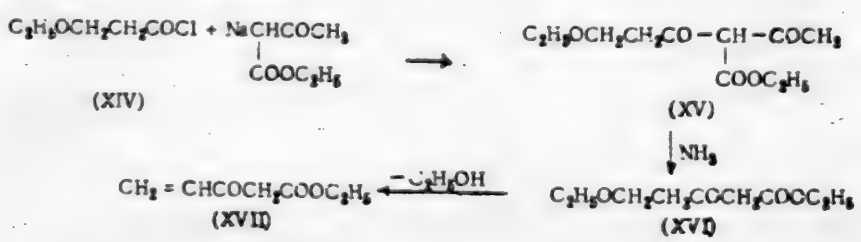
We also tried to synthesize the bicyclic compounds by another method. We subjected dimedon and dihydroresorcinol to the action of 1-diethylamino-3-ketobutane (XIII) at 70-80°. In the case of dimedon, however, we only succeeded in obtaining the above-mentioned mono-adduct (X), while in the case of dihydroresorcinol a complex mixture is obtained from which a carboxylic acid of unknown structure was isolated.

On the other hand, heating of 1-diethylamino-3-ketobutane (XIII) with methyldihydroresorcinol leads directly to formation of 9-methyl-1,6-diketo-$\Delta^{9(10)}$-octalin (IV). This transformation proceeds through the stage of triketone (III) which cyclizes under the influence of diethylamine during the reaction.



(II) (XIII) (III) (IV)

The preparation of 5-carbethoxy-9-methyl-1,6-diketodecalin (XX) required carbethoxymethylvinyl ketone (XVII), whose synthesis was effected by the following scheme:

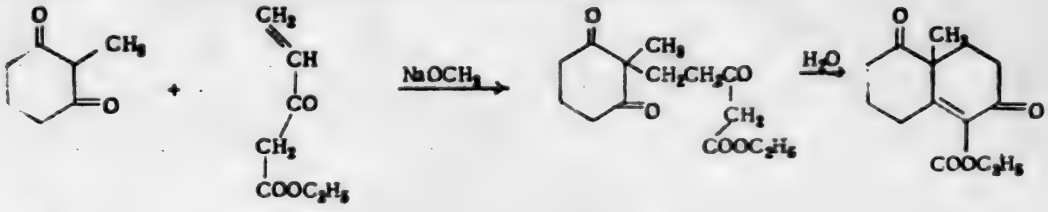


(XIV) (XV) (XVII) (XVI)

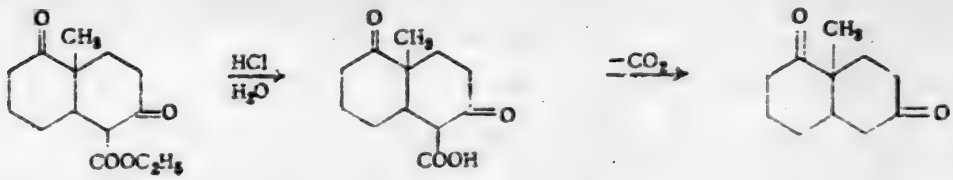
β-Ethoxypropionyl chloride (XIV) reacts with sodium ethylacetoacetate to give the diacyl derivative (XV) which with ammonia undergoes ammonolysis with formation of ethyl γ-(ethoxymethyl)-acetoacetate (XVI).

Distillation of the latter in vacuum in presence of p-toluenesulfonic acid causes cleavage of a molecule of alcohol with formation of vinylcarbethoxymethyl ketone (XVII). Its reaction with methyldihydroresorcinol, which proceeds in presence of sodium methylate with considerable evolution of heat, gives, in addition to the triketo ester (XVIII), the bicyclic diketo ester (XIX). This occurrence of cyclization in the conditions of condensation cannot be regarded as unexpected, for in this case ring closure is facilitated by the presence of an active methylene group in the molecule of the triketo ester (XVIII).

The triketo ester (XVIII) is a pure keto form, since in the cold it does not give a coloration with iron chloride. The triketo ester (XVIII) readily cyclizes when heated with formation of the unsaturated diketo ester (XIX) which, in presence of platinum catalyst is hydrogenated to 5-carbethoxy-9-methyl-1,6-diketodecalin (XX). Structure of the latter was confirmed by subjecting it to saponification and decarboxylation, when a diketone was obtained which was identical with the previously described cis-9-methyl-1,6-diketodecalin (XXI).



(II) (XVII) (XVIII) (XIX)



(XX) (XXI)

In order to introduce the carbomethoxyethyl group into the 5-position of the diketooctalin (IV), we started from (γ-carbomethoxypropyl)-vinyl ketone (XXV), which we synthesized by two methods.

The hydrochloride of γ-(β'-piperidinopropionyl)-butyric acid (XXII) is treated in a medium of methanol with dry hydrogen chloride. The resultant amino ester (XXIII) is transformed into the methiodide (XXIV) which is then subjected to dry distillation.

$$HCl \cdot C_5H_{10}NCH_2CH_2COCH_2CH_2CH_2COOH \xrightarrow[HCl]{CH_3OH} C_5H_{10}NCH_2CH_2COCH_2CH_2CH_2COOCH_3$$

(XXII) (XXIII)

$$CH_2=CHCOCH_2CH_2CH_2COOCH_3 \leftarrow CH_3I \cdot C_5H_{10}NCH_2CH_2COCH_2CH_2CH_2COOCH_3 \quad (CH_3I \downarrow)$$

(XXV) (XXIV)

In the second method, γ-(ethoxymethyl)-acetoacetic ester (XVI) in presence of sodium methylate is condensed with acrylic ester and the reaction product (XXVI) is saponified and decarboxylated by boiling with hydrochloric acid. The keto acid (XXVII) is esterified with methyl alcohol in presence of hydrogen chloride and the resultant ester (XXVIII) is distilled in vacuum with a small quantity of p-toluenesulfonic acid.

$$C_2H_5OCH_2CH_2COCH_2COOC_2H_5 \xrightarrow[CH_3ONa]{CH=CHCOOCH_3} C_2H_5OCH_2CH_2COCHCH_2CH_2COOCH_3$$

(XVI) (XXVI)

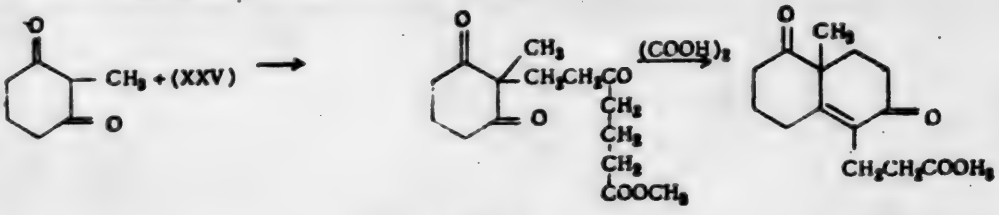
$$C_2H_5OCH_2CH_2COCH_2CH_2COOCH_3 \xleftarrow[HCl]{CH_3OH} C_2H_5OCH_2CH_2COCH_2CH_2CH_2COOH$$

(XXVIII) (XXVII)

$$\downarrow -C_2H_5OH \ (C_7H_7SO_3H)$$

$$CH_2=CHCOCH_2CH_2CH_2COOCH_3 \ (XXV)$$

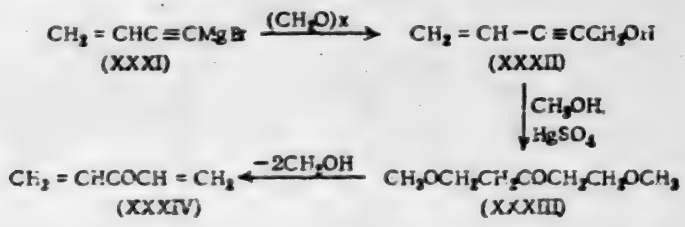
(γ-Carbomethoxypropyl)-vinyl ketone (XXV) adds on to methyldihydroresorcinol under the influence of sodium methylate in methanol solution. Heating of the reaction product (XXIX) in vacuum with oxalic acids gives a crystalline substance with a neutral reaction whose elementary composition exactly corresponds to the bicyclic compound (XXX). It is interesting to note that the triketo ester (XXIX), unlike the triketone (III), does not undergo cyclization when heated with salts of secondary amines at 90-95°.



(XXIX) (XXX)

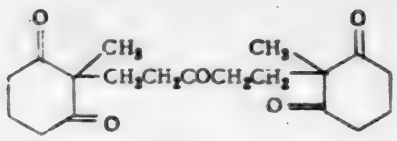
The reaction of methyldihydroresorcinol (II) with divinyl ketone (XXXIV) could also be of interest for the synthesis of polycyclic compounds related to the steroids.

Divinyl ketone (XXXIV) was synthesized by the method of N. I. Nazarov and I. V. Torgov [3] by reaction of vinylacetylenemagnesium bromide (XXXI) with formaldehyde, followed by isomerization of the carbinol (XXXII) and cleavage of methanol from the dimethoxy ketone (XXXIII).

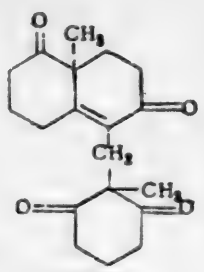


In the course of this reaction we established that vinylacetylenemagnesium bromide reacts not only with gaseous formaldehyde but also with solid paraformaldehyde, which greatly simplifies the performance of the synthesis.

Addition of methyldihydroresorcinol in ordinary conditions to divinyl ketone (XXXIV) gives a crystalline bis-adduct (XXXV). Due, however, to the instability of the substance we were unable to effect its cyclization to the tricyclic ketone (XXXVI)



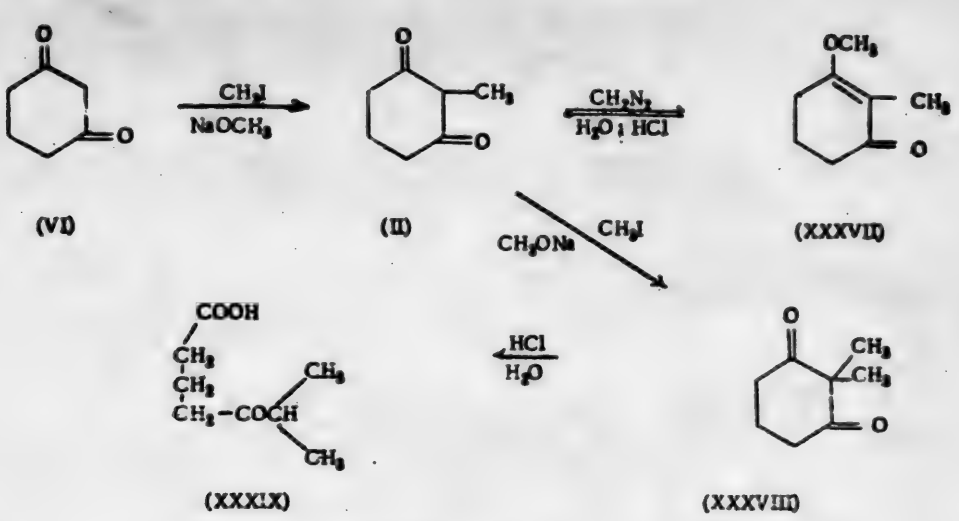
(XXXV)



(XXXVI)

The methyldihydroresorcinol used in the above-described investigations was prepared by us by methylation of dihydroresorcinol (VI). A closer study of this reaction showed that the low yield of methyldihydroresorcinol (II) was connected with the formation of the dimethyl derivative (XXXVIII). The structure of the latter was confirmed by hydrolytic cleavage to the known γ-isobutyrylbutyric acid (XXXIX) [4] and by comparison of its properties with those of the isomeric enolic methyl ether (XXXVII), which can also be formed in the process of methylation. We showed that the enolic ether (XXXVII), prepared by the action of diazomethane on methyldihydroresorcinol, gives

on saponification not the carboxylic acid (XXXIX), but the original diketone (II).



EXPERIMENTAL

Methylvinyl ketone (I) (b.p. 79-80°, n_D^{20} 1.4460) was prepared by hydration of vinylacetylene [5].

γ-(β'-Piperidiniopropionyl)butyric acid hydrochloride (XXII) (m.p. 158-159°) [6] was prepared by reaction of γ-acetylbutyric acid with formaldehyde and piperidine hydrochloride.

Dihydroresorcinol (VI) (m.p. 104-105°) was prepared by hydrogenation of resorcinol [7].

Dimedon (IX) (m.p. 144-145°) was synthesized by reaction of malonic ester with mesityl oxide, followed by saponification of the product of cyclization [8].

Divinyl ketone (XXXIV) was obtained by cleavage of alcohol from β,β'-dimethoxydiethyl ketone and was utilized in the form of a methanol solution (b.p. 25-40° at 70 mm) [3].

β-Ethoxypropionyl chloride (XIV) (b.p. 62-64° at 30 mm) was prepared from β-ethoxypropionic acid and thionyl chloride [9].

Methylation of dihydroresorcinol. To a solution of sodium methylate, prepared from 2.3 g sodium and 25 ml dry methanol, was added with stirring, 11.2 g dihydroresorcinol (VI) followed by 16 g methyl iodide. After heat development had ceased, the mixture was boiled on a water bath for 3 hours. The methanol was driven off in vacuum and 10 ml water was added to the residue. The resultant crystalline precipitate was drained and washed with water. Yield 5 g methyldihydroresorcinol (II) with m.p. 208-209° (from aqueous ethanol).

The filtrate remaining after separation of the methyldihydroresorcinol was extracted 5 times with chloroform; the chloroform solution was evaporated to dryness and the residue fractionated in vacuum to give 0.7 g dimethyldihydroresorcinol (XXXVIII) with b.p. 98-100° at 39-40° at 10 mm (from ligroine).

Found %: C 68.19, 68.40; H 8.56, 8.53. $C_8H_{12}O_2$. Calculated %: C 68.5; H 8.6

Hydrolytic cleavage of dimethyldihydroresorcinol. 3 g dimethyldihydroresorcinol (XXXVIII) and 20 ml diluted (1 : 1) hydrochloric acid were heated on a boiling water bath for 2 hours. The mixture was extracted with ether, and after removal of the ether the residue was distilled in vacuum to give 2 g γ-isobutyrylbutyric acid (XXXIX) with b.p. 143-146° at 4 mm; n_D^{21} 1.4449.

The semicarbazone melted at 183-184° with decomposition (from methanol). The literature gives m.p. 185-185.5° (with decomposition) [4].

Preparation of the methyl ether of methyldihydroresorcinol (XXXVII). To a suspension of 3 g methyldihydroresorcinol (II) in 10 ml ether was added a 3% ethereal solution of diazomethane until the substance dissolved completely. After removal of the solvent the residue was distilled in vacuum.

Yield 2.8 g methyl ether of methyldihydroresorcinol (XXXVII) with b.p. 98-99° at 3 mm; m.p. 43-44° (from n-hexane).

Found %: C 68.15, 68.26; H 8.83, 8.80; $C_9H_{12}O_3$. Calculated %: C 68.5; H 8.6.

Treatment of the ether of the enol (XXXVII) with dilute hydrochloric acid (1 : 1) in the cold quantitatively converted it into methyldihydroresorcinol (II), m.p. 208-209°.

Condensation of methylvinyl ketone with dihydroresorcinol. To a solution of 1 g KOH in 8 ml methanol was added 11 g dihydroresorcinol (VI) and 20 g methylvinyl ketone in 80 ml methanol. The mixture was boiled on a water bath for 3 hours. After the methanol had been taken off in vacuum the residue was mixed with 20 ml saturated potassium carbonate solution and extracted with chloroform. The chloroform solution was evaporated to dryness and the neutral reaction product fractionated in vacuum to give 9 g di-(γ-ketobutyl)-dihydroresorcinol (VIII) with b.p. 140-143° at 0.5 mm, m.p. 123-124° (from aqueous methanol).

Found %: C 66.79, 66.78; H 7.92, 7.99. $C_{16}H_{24}O_4$. Calculated %: C 66.6; H 7.9.

The alkaline solution remaining after the extraction was acidified with concentrated hydrochloric acid (to Congo) and extracted with chloroform. After removal of the solvent the residue was distilled in vacuum to give 7 g (γ-ketobutyl)-dihydroresorcinol (VII) with b.p. 137-140° at 0.2 mm; n_D^{20} 1.5400.

Found %: C 66.00, 66.15; H 7.70, 7.65. $C_{10}H_{14}O_3$. Calculated %: C 65.9; H 7.5.

The substance possesses well-marked acidic properties, gives a dark-violet coloration with iron chloride and displaces carbonic acid from its salts.

Reaction of (γ-ketobutyl)-dihydroresorcinol with methylvinyl ketone. To a solution of 0.1 g KOH in 2 ml methanol is added 2 g (γ-ketobutyl)-dihydroresorcinol (VII) followed by 2 g methylvinyl ketone in 8 ml methanol. The mixture is boiled on the water bath for 3 hours. After driving off the methanol in vacuum, the residue is worked up with saturated potassium carbonate solution and extracted with chloroform. After removal of the solvent, the residue crystallized. Yield 1 g of substance with m.p. 123-124° (from aqueous methanol), which did not give a depression with the above-described di-(γ-ketobutyl)-dihydroresorcinol (VIII).

Condensation of methylvinyl ketone with dimedon. To a solution of 1 g KOH in 8 ml methanol was added 14 g dimedon (IX) and 20 g methylvinyl ketone in 80 ml methanol. The mixture was boiled on the water bath for 3 hours. After working up in the usual manner, the neutral portion yielded 12 g di-(γ-ketobutyl)-dimedon (XI) with m.p. 106-107° (from aqueous methanol).

Found %: C 68.60, 68.49; H 8.84, 8.67. $C_{18}H_{26}O_4$. Calculated %: C 68.6; H 8.6.

From the acidic products was isolated 11 g γ-ketobutyldimedon (X) with m.p. 100-101° (from aqueous methanol).

Found %: C 68.68, 68.71; H 8.75, 8.76. $C_{12}H_{18}O_3$. Calculated %: C 68.6; H 8.6

Reaction of substance (X) with methylvinyl ketone gives the bis-adduct (XI).

Transformation of di-(γ-ketobutyl)-dimedon (XI) into the mono-adduct (X). 2 g di-(γ-ketobutyl)-dimedon (XI) and a solution of 2 g potassium carbonate in 8 ml water were subjected to slow distillation at atmospheric pressure. Methylvinyl ketone (m.p. of semicarbazone 140-141°) was detected in the distillate. The operation was interrupted when 2 g solution remained in the distilling flask. This residue was made acid to Congo with dilute hydrochloric acid (1 : 1) and the precipitate was recrystallized from aqueous methanol. Yield 0.8 g substance with m.p. 100-101°, which did not give a depression with the mono-adduct (X).

Preparation of the methyl ether of (γ-ketobutyl)-dimedon (XII). To 8 g (γ-ketobutyl)-dimedon (X) with stirring was added a 3% ethereal solution of diazomethane until nitrogen ceased to come off. After driving off the solvent, the residue was distilled in vacuum.

There was obtained 7 g methyl ether of (γ-ketobutyl)-dimedon (XII) with b.p. 148-151° at 2 mm, m.p. 75-76° (from ligroine-benzene mixture).

Found %: C 69.73, 69.61; H 8.97, 8.96. $C_{13}H_{20}O_3$. Calculated %: C 69.6; H 8.9.

On heating with dilute (1 : 1) hydrochloric acid, the substance was entirely transformed into (γ-ketobutyl)-dimedon (X).

Reaction of 1-diethylamino-3-ketobutane with dimedon. A mixture of 7 g dimedon (IX) and 14 g of 1-diethylamino-3-ketobutane (XIII) was heated on a water bath at 90° for 2 hours. While cooling with ice, the reaction mass was treated with dilute hydrochloric acid (1 : 1) until acid to Congo, and the resultant crystals were drained

and washed with benzene to give 2 g with m.p. 100-101° (from aqueous methanol), which did not give a depression with (γ-ketobutyl)-dimedon (X).

Reaction of 1-diethylamino-3-ketobutane with dihydroresorcinol. A solution of 5.3 g dihydroresorcinol (VI) and 7 g 1-diethylamino-3-ketobutane (XIII) in 50 ml dry benzene was subjected to distillation at atmospheric pressure. After driving off 40 ml of the solvent, the residue was made acid to Congo with dilute hydrochloric acid (1: 1) and extracted with benzene. After removal of the solvent, the residue partly crystallized. Yield 1.5 g acid with m.p. 162-163° (from aqueous methanol).

Found %: C 71.38, 71.29; H 7.92, 8.07 g-equiv. 234. $C_{14}H_{18}O_5$. Calculated %: C 71.7; H 7.7 g-equiv. 235.

On hydrogenation with Pt catalyst in methanol, the substance absorbs 1 mole hydrogen.

Reaction of 1-diethylamino-3-ketobutane with methyldihydroresorcinol. A mixture of 3 g methyldihydroresorcinol (II) and 5 g 1-diethylamino-3-ketobutane (XIII) was heated on a water bath at 80-90° for 2 hours. After treatment with dilute hydrochloric acid (1 : 1) and extraction with benzene the product of reaction was fractionated in vacuum to give 0.3 g substance with m.p. 48-50°, which did not give a depression with authentic 9-methyl-1,6-diketo-$\Delta^{8(10)}$-octalin (IV) [1].

Preparation of γ-(ethoxymethyl)-acetoacetic ester (XVI). To a suspension of sodium ethylacetoacetate, prepared from 2.3 g sodium, 13 g ethylacetoacetate and 70 ml absolute ether, dropwise addition was made of 14 g β-ethoxypropionyl chloride in 14 ml absolute ether with cooling (iced water) and stirring. The reaction mixture was left at room temperature for 24 hours and then, after separation of the sodium chloride, saturated with dry ammonia while being cooled with ice. The ethereal solution was washed with dilute hydrochloric acid (1 : 1) and then with 5% sodium carbonate solution. After removal of solvent, it was subjected to fractional distillation in vacuum to give 4.5 g γ-(ethoxymethyl)-acetoacetic ester (XVI) with b.p. 80-84° at 2 mm; n_D^{21} .4361.

Found %: C 56.92, 57.01; H 8.55, 8.33; $C_9H_{16}O_4$. Calculated %: C 57.4; H 8.5.

Carbethoxymethylvinyl ketone (XVII). 3 g γ-(ethoxymethyl)-acetoacetic ester (XVI) and 0.04 g p-toluenesulfonic acid were subjected to distillation in vacuum at 18-20 mm. The temperature was held at 120-130°. In these conditions cleavage of the alcohol gradually took place and the reaction product distilled over. Yield 1.8 g carbethoxymethylvinyl ketone (XVII) with b.p. 76-78° at 18 mm; n_D^{20} 1.4585.

Found %: C 58.97, 59.24; H 6.59, 6.72. $C_7H_{10}O_3$. Calculated %: C 59.0; H 7.0.

On prolonged standing the substance polymerizes to a transparent vitreous mass.

Reaction of carbethoxymethylvinyl ketone with methyldihydroresorcinol. To a solution of sodium methylate, prepared from 0.05 g sodium and 15 ml absolute methanol, was added 6.5 g methyldihydroresorcinol (II) followed, with energetic stirring, by 7.5 g carbethoxymethylvinyl ketone (XVII). The mixture began to heat up and continued to do so for about 30 minutes. The reaction was completed by heating on a water bath at 50-55° for 30 minutes. After removal of the methanol in vacuum, the residue was worked up with a solution of 3 g sodium carbonate in 10 ml water and extracted with benzene. The solvent-free reaction product crystallized. Yield 4 g of triketoester (XVIII) with m.p. 113-114° (from methanol).

Found %: C 62.49, 62.52; H 7.64, 7.44. $C_{14}H_{20}O_5$. Calculated %: C 62.7; H 7.5.

In the cold the compound does not give a reaction with iron chloride; on heating to 50-60° a cherry-red color appears.

The mother liquor (6 g) remaining after separation of the crystals of triketoester (XVIII) was distilled in vacuum to give 3.8 g of the bicyclic ester (XIX) with b p. 179-180° at 0.5 mm; n_D^{22} 1.5208.

Found %: C 66.61, 66.53; H 6.91, 7.18; $C_{14}H_{18}O_4$. Calculated %: C 67.2; H 7.2.

The substance gives a coloration with iron chloride; the 2,4-dinitrophenylhydrazone melts at 208-210° (with decomposition).

Cyclization of the triketoester (XVIII). 4 g of triketoester (XVIII) was distilled in vacuum to give 2 g bicyclic ester (XIX) with b.p. 178-183° at 0.5 mm; n_D^{20} 1.5250.

Found %: C 66.65, 66.84; H 6.96, 7.20. $C_{14}H_{18}O_4$. Calculated %: C 67.2; H 7.2.

The 2,4-dinitrophenylhydrazone melted at 208-210° (with decomposition).

Found %: N 15.35, 15.15. $C_{25}H_{22}O_7N_4$. Calculated %: N 13.1.

Hydrogenation of the bicyclic ester (XIX). 2 g bicyclic ester (XIX) was hydrogenated in 5 ml methanol in presence of platinum oxide at room temperature and normal pressure. In the course of an hour 18 ml hydrogen (1 mole) was absorbed, after which hydrogenation substantially ceased. After freeing from catalyst and solvent, the reaction product was fractionated in vacuum to give 1.2 g 9-methyl-1,6-diketo-5-carbethoxydecalin (XX) with b.p. 158-162° at 1 mm; n_D^{20} 1.5168.

Found %: C 67.06, 66.80; H 8.11, 8.12. $C_{14}H_{20}O_4$. Calculated %: C 66.6; H 7.9.

Saponification of 9-methyl-1,6-diketo-5-carbethoxydecalin (XX). 1.3 g 9-methyl-1,6-diketo-5-carbethoxydecalin (XX) and 20 ml dilute hydrochloric acid (1 : 1) were refluxed for 6 hours. After removal of the volatile products in vacuum, there was a residue of 0.8 g viscous oil from which was obtained 0.3 g of a semicarbazone with m.p. 222-223° (with decomposition), not giving a depression with the bis-semicarbazone of authentic cis-9-methyl-1,6-diketodecalin (XXI) [2]. Decomposition of the semicarbazone with hydrochloric acid yielded the 9-methyl-1,6-diketodecalin itself (XX) with m.p. 65-67° and not giving a depression with an authentic specimen [2].

Preparation of (γ-carbomethoxypropyl)-vinyl ketone (XXV). 1) Into a mixture of 40 g γ-(β'-piperidinopropionyl)-butyric acid hydrochloride (XXII) and 250 ml dry methanol was passed a stream of dry hydrogen chloride until the solution was saturated. After driving off the excess of alcohol and hydrogen chloride in a low vacuum, the residue was treated (while cooling) with a solution of 20 g NaOH in 50 ml water and extracted with ether. The ethereal solution was mixed with 60 g methyl iodide and stood for 6 hours at room temperature before evaporating to dryness on a water bath. The residual methiodide was subjected to distillation in vacuum. Yield 15 g (γ-carbomethoxypropyl)-vinyl ketone (XXV) with b.p. 70-71° at 2 mm; n_D^{22} 1.4481.

Found %: C 61.37, 61.51; H 7.97, 7.99. $C_8H_{12}O_3$. Calculated %: C 61.5; H 7.7.

The semicarbazone melts at 187-188°.

Found %: N 19.53, 19.62; $C_9H_{15}O_3N_3$. Calculated %: N 19.7.

2) To a solution of the sodium derivative prepared from 5 g γ-(ethoxymethyl)-acetoacetic ester (XVI) and 0.2 g sodium, was added 2 g methyl acrylate and the mixture heated for 4 hours at 60-65°. The product of condensation was isolated by saponification by boiling for 5 hours with 20 ml dilute hydrochloric acid (1 : 1). After removal of the volatiles in vacuum, the residue was dissolved in 10 ml methanol and the solution saturated with dry hydrogen chloride before evaporating to dryness in vacuum. The reaction products were distilled at 15 mm in presence of a small amount of p-toluenesulfonic acid. Yield 0.7 g (γ-carbomethoxypropyl)-vinyl ketone (XXV) with b.p. 102-105° at 15 mm; n_D^{25} 1.4490

The semicarbazone melted at 187-188°.

Preparation of 9-methyl-1,6-diketo-5-(β-carbomethoxyethyl)-$\Delta^{5(10)}$-octalin (XXX). To a solution of sodium methylate, prepared from 0.1 g sodium and 15 ml dry methanol, was added 8.7 g methyldihydroresorcinol (II) and 10 g (γ-carbomethoxypropyl)-vinyl ketone (XXV). The mixture was boiled on a water bath for 6 hours. The solvent was taken off in vacuum and the residue worked up with sodium carbonate solution and extracted with ether. Removal of the latter left 15 g viscous oil (n_D^{22} 1.4860), not distilling without decomposition even in high vacuum. 3 g of the crude condensation product and 1 g oxalic acid were heated at 140-150° for 2 1/2 hours. After cooling, the mixture was worked up with 2 g sodium carbonate and 20 ml water; the crystals were drained and washed with ether. Fractional crystallization from benzene gave 0.4 g 9-methyl-1,6-diketo-5-(β-carbomethoxyethyl)-$\Delta^{5(10)}$-octalin (XXX) with m.p. 168-169°.

Found %: C 68.11, 67.94; H 7.41, 7.31. $C_{15}H_{22}O_4$. Calculated %: C 68.2, H 7.6.

Preparation of vinylethinylcarbinol (XXXII). Into a Grignard solution, prepared from 25 g magnesium, 110 g ethyl bromide and 400 ml absolute ether, was passed 65 g dry vinylacetylene. Then with cooling (ice water) and energetic stirring, 50 g finely crushed paraformaldehyde was introduced in portions. The temperature was held at 25-30° by external cooling. After standing for 12 hours at room temperature, the mixture was worked up with ice and dilute hydrochloric acid (1 : 1). The ether layer was separated and dried with sodium sulfate; the ether was driven off and the residue distilled in vacuum to give 35 g vinylethinylcarbinol (XXXII) with b.p. 57-59° at 12 mm; n_D^{25} 1.4935

Reaction of divinyl ketone with methyldihydroresorcinol. To a solution of sodium methylate, prepared from 0.05 g sodium and 5 ml dry methanol, was added 7 g methyldihydroresorcinol (II) and 2 g divinyl ketone (XXXIV) in 2 ml methanol. The mixture was boiled on a water bath for 3 hours and then evaporated in a vacuum at 50-60°.

The residue was worked up with sodium carbonate solution and extracted with chloroform. After removal of the solvent the residue partly crystallized to give 1.7 g of bis-adduct (XXXV) with m.p. 100-101° (from aqueous methanol).

Found %: C 68.17, 68.22; H 7.82, 7.75. $C_{19}H_{28}O_5$. Calculated %: C 68.2; H 7.8

SUMMARY

1. It is shown that condensation of dihydroresorcinol (VI) and dimedon (IX) with methylvinyl ketone leads to a mixture of mono- and diketobutyl derivatives (VII, VIII, X, XI). The action of various cyclizing media upon the mono-ketobutyl derivatives (VII, X) failed to give the corresponding bicyclic diketones (1,6-diketooctalins).

2. It was established that in the reaction of 1-diethylamino-3-ketobutane (XIII) with dimedon formation takes place of the monoketobutyl derivative (X), while the reaction of the same ketoamine with methyldihydroresorcinol (II) gives 9-methyl-1,6-diketo-$\Delta^{9(10)}$-octalin (IV).

3. Methods are described for the preparation of carbethoxymethylvinyl ketone (XVII) and (γ-carbomethoxypropyl)-vinyl ketone (XXV). Their condensation was effected with methyldihydroresorcinol, leading to ring-closure to form the substituted diketooctalins (XIX, XXX).

4. It was established that the bis-adduct (XXXV) is formed in the reaction of divinyl ketone with methyldihydroresorcinol.

5. The methylation of dihydroresorcinol was studied and it was observed that the dimethyl derivative (XXXVIII) is formed side by side with methyldihydroresorcinol.

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THE SULFONATION REACTION

XXXI. THE INITIAL RATIOS OF NAPHTHALENEDISULFONIC ACIDS

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It is known that in the sulfonation of naphthalene to monosulfonic acids, two isomers are always obtained, one of which—depending upon the temperature and the duration of sulfonation—predominates. There are no conflicting statements in the literature about the quantities of isomers formed at high temperatures (130-165°), but the data about the ratios of isomers formed at temperatures of 0 to 60°, i.e. when their isomerization has not yet taken place, are extremely conflicting.

Thus, Fierz-David [1] considers that below 40° 4% β-sulfonic acids and 96% α-acids are formed. According to Lantz [2] at 20 to 60° 11-13% β-sulfonic acids are formed. According to the data of works analyses [3], the content of the β-isomer reaches 15%. At 7 to 80°, Perelman [4] obtained 15-18% β-sulfonic acids.

While not concerning ourselves at all with the problem of the formation of isomeric disulfonic acids, we set forth the literature data on the amounts of isomers which are formed at low temperatures, i.e. when they do not yet undergo isomerization.

Fierz-David and Hasler [5] point out that sulfonation of naphthalene at 40° gives about 25% 1,6-disulfonic acid and 70% 1,5-disulfonic acid. Ufimtsev and Krivoshlykova [6] sulfonated naphthalene-β-sulfonic acid at the ordinary temperature and obtained about 20% 1,7-disulfonic acid and 80% 1,6-disulfonic acid. According to the data of works analyses [3], the ratio of 1,5- to 1,6-isomer resulting from sulfonation of naphthalene at 20-60° is 65:35. At the Dorogomilov plant [9] operation at a sulfonation temperature of 25° gave 71-72% 1,5-disulfonic acid; with a higher sulfonation temperature up to 65°, the amount of 1,5-isomer was found to be 60%. Lantz [10] found that in sulfonation of α-sulfonic acid at low temperatures there is formed 77% 1,5-acid together with an unknown acid (apparently 1,7-disulfonic acid) and 23% 1,6-acid. Sulfonation of β-acid gave 70% 1,6-acid, 16% x-acid (probably 1,7-) and 7% each of 2,6- and 2,7-isomers. However, Lantz made the qualification that the measurements were not carried out with the accuracy needed for quantitative study and that methods of analysis were employed which were only suitable for mixtures containing not more than three disulfonic acids. Fierz-David and Richter [11] also sulfonated the β-acid and found in the sulfonated mixture 20% 1,7-disulfonic acid and 80% 1,6-acid.

The composition of the sulfonated mixture obtained by the action of chlorosulfonic acid on naphthalene has scarcely been studied. Armstrong [12] was of the opinion that only the 1,5-disulfonic acid is obtained. V. M. Rodionov [13] obtained 88% of the theoretical yield of unpurified 1,5-disulfochloride, while Pollak and co-workers [14] obtained 59%. The literature does not mention whether and in what quantities other isomers are formed by the action of chlorosulfonic acid upon naphthalene.

In this investigation, we undertook to establish the content of α- and β-isomers obtained by monosulfonation of naphthalene and then, after sulfonating the α- and β-sulfonic acids, to determine the amounts of disulfonic acids formed and to calculate the initial ratios of disulfonic isomers which are formed on sulfonation of naphthalene in conditions in which isomerization has not yet taken place.

EXPERIMENTAL

Monosulfonation of naphthalene was performed at temperatures of 0 and 57°, i.e. below the temperature (70°) at which the α-acid begins to hydrolyze [15]. The reaction was carried out in a hermetically closed broad test tube fitted with a tube and a ground-glass stopper into which was fused a narrow tube. Attached to the latter was a rubber tube through which passed a stirrer tightly fitting into the rubber tube.

To a weighed amount of naphthalene with cooling and stirring, sulfuric acid was added, dropwise, through the tube in the course of ten minutes, and the mixture was then stirred for 10 hours. After solution in water, the unreacted naphthalene was separated and determined by the method previously described by one of us [15]. The total acidity of the filtrate was determined; from the amount of residual naphthalene, the sulfuric acid taken and the total acidity, the amount of monosulfonic acids in the mixture was calculated. The discrepancies in the amount of monosulfonic acids found on the basis of the naphthalene and on the basis of the change of acidity fluctuated within the

range of 0.2.-1% and demonstrated the absence of disulfonic acids. The content of α-acid was determined by precipitation with m-nitro-o-anisidine [16].

The experimental results, set forth in Table 1, showed that 85% of α-isomer is obtained regardless of whether the sulfonation is performed at 0 or 57°.

TABLE 1

Sulfonation of Naphthalene with 99.8 % Sulfuric Acid over a Period of 10 hours

Expt. No.	Moles H_2SO_4 taken per mole naphthalene	Temp. (°C)	Found	
			Conc. of sulfuric acid in mixture (%)	α-acid in % of sum of monosulfonic acids (%)
270	2.071	0-1	94.2	85.0
271	2.003	0-1	93.5	85.3
272	2.044	56-57	89.2	85.5
274	1.701	56-57	86.8	85.2

Sulfonation of α-naphthalenesulfonic acid. A weighed amount of the dihydrate of the α-acid was dried in the same vessel in vacuum over phosphorus pentoxide at 76-78° until nearly the whole of the water was lost; then, with cooling and stirring, oleum was added from a dropping funnel through the tube. The residues of oleum on the walls of the funnel were washed into another vessel and titrated; the tube was closed and the vessel kept for 12 hours at room temperature and for 5 hours at 56-57° with periodic stirring. The weight of the vessel after the experiment confirmed its hermeticity. A portion of the sulfo mass was then analyzed by the method of exhaustive sulfonation which we previously described [17], while the residual amount was dissolved in a measuring flask for determination of the total acidity and the content of 1,5-isomer by the benzidine and xylidine method [18].

The experimental results, set forth in Table 2, showed that sulfonation of the α-acid gives (in round figures): 75% 1,5-disulfonic acid, 10% 1,6-disulfonic acid, 15% 1,3- and 1,7-disulfonic acids.

The formation of 1,7-disulfonic acid on sulfonation of the α-acid had not previously been reported. The amount of 1,3-isomer is considerably less than the amount of 1,7-isomer.

TABLE 2

Sulfonation of α-Naphthalenesulfonic Acid at 56-57° in the Course of 5 hours with 20.4% Oleum

Expt. No.	Moles free SO_3 taken per mole α-acid	Found (in % of sum of sulfonic acids)					Remarks
		α-acid	1,5-acid		1,6-acid	1,3- and 1,7-acids	
			by benzidine method	by xylidine method			
282	0.775	0.3	74.3	74.1	9.4	16.1	We assume that the α-acid is transformed by exhaustive sulfonation into tetrasulfonic acid
284	0.801	1.3	73.3	75.1	10.1	14.4	
291	0.789	0.9	72.3	74.2	9.8	16.0	

Sulfonation of β-naphthalenesulfonic acid was carried out by the same procedure as for the sulfonation of the α-acid, except that the oleum was introduced in such quantity that the free sulfur trioxide was only sufficient for binding the water of crystallization of the sulfonic acid (1 mole). The sulfo mixture was analyzed by the indicated methods [17, 18]. In the sulfonation of β-acid, the formation is possible of α,β- and β,β-isomers, while formation of 1,5-acid is impossible. In the determination of 2,7-acid in the form of benzidinesulfonate the 1,6-isomer was isolated as well as the 2,7-isomer. This prompted us to double the dilution of the solutions in comparison with the previous instructions and led to a very large correction for the loss of 2,7-isomer.

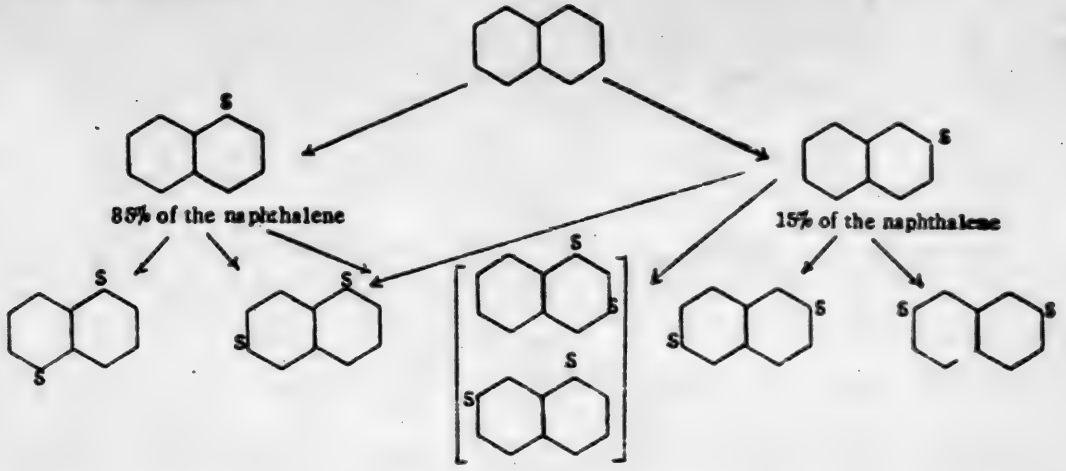
The results of the experiments, set forth in Table 3, showed that sulfonation of the β-acid gives (in round figures): 67% 1,6-disulfonic acid, 21% 1,3- and 1,7-disulfonic acids, 11% 2,7-disulfonic acid and 1% 2,6-disulfonic acid.

TABLE 3

Sulfonation of β-Naphthalenesulfonic Acid at 56-57° in the Course of 5 hours with 99.5% Sulfuric Acid

Expt. No.	Moles H_2SO_4 taken per mole β-acid	Found (in % of total sulfonic acids)					Remarks
		Trisulfonic acids	2,6-acid	2,7-acid	1,6-acid	1,3-and 1,7-acids	
290	4.833	1.2	1.1	12.4	63.8	21.5	We assume that exhaustive sulfonation of the trisulfonic acids gives 50% tetrasulfonic acids.
292	5.838	3.6	1.2	10.3	65.7	19.2	

The data for the composition of the sulfonic acid mixtures obtained on sulfonation of the α- and β-acids permit calculation of the composition of the disulfonic mixtures obtained by direct sulfonation of naphthalene and in the absence of isomerization. The disulfonic mixture obtained by sulfonation of naphthalene contains: 64% 1,5-disulfonic acid, 18% 1,6-disulfonic acid, 16% 1,3- and 1,7-disulfonic acids, 1.7% 2,7-disulfonic acid, 0.2% 2,6-disulfonic acid (see scheme)*



75% of α-isomer	10% of α-isomer	15% of α-isomer	0% of α-isomer	0% of α-isomer
0% of β-isomer	67% of β-isomer	21% of β-isomer	1% of β-isomer	11% of β-isomer
63.7% of naphthalene	18.6% of naphthalene	16.3% of naphthalene	0.2% of naphthalene	1.7% of naphthalene

The experiments on the sulfonation of naphthalene and its monosulfonic acids consequently show that the isomer most labile toward hydrolysis is formed predominantly. Thus from naphthalene we get mainly α-acid; from α-acid mainly 1,5-disulfonic acid; from β-acid 1,6-disulfonic acid. This rule can also be extended to β,β-isomers from which always more of the more labile 2,7-isomer than of the 2,6-isomer appears in the sulfonic mixture; in conditions of absence of their hydrolysis the ratio of 2,6- to 2,7-isomer is 1:8.5.

SUMMARY

The ratio of α- and β-naphthalenesulfonic acids formed by sulfonation of naphthalene at low temperatures was determined. Sulfonation of α- and β-sulfonic acid at low temperature (57°) was followed by determination of the amount of sulfonic acids formed in each case.

The composition was calculated of the disulfonic acid mixture obtained on direct sulfonation of naphthalene in conditions of absence of isomerization.

It is shown that the isomers which are the most labile of all to hydrolysis are formed in preponderance.

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SYNTHESIS OF DERIVATIVES OF SERINE PEPTIDES

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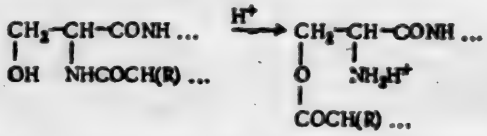
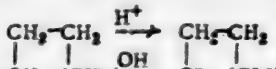
It was previously established [1] that the peptide bonds in protein, formed at the amino group of β-hydroxamino acids, are hydrolyzed considerably more easily than others. It was shown (indirectly) that this phenomenon is evidently associated with previous rearrangement of N-peptides of β-hydroxamino acids into O-peptides, which then easily hydrolyze.



Considering that such processes may take place not only during acidic hydrolysis of proteins but also in the animal organism, we decided that a study of the phenomenon of migration of the aminoacyl residue in the peptides of serine was desirable.

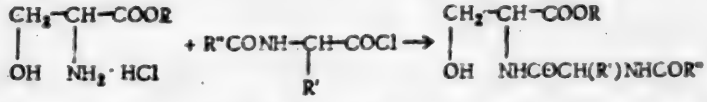
The ability of the aminoacyl residue to migrate from nitrogen to oxygen and from oxygen to nitrogen was recently demonstrated by us for the case of ethanolamine [2]



where R = $COCH_2NHCOC_6H_5$, $COCH(CH_2C_6H_5)NHCOC_6H_5$, $COCH_2NHCOCH_2NHCOC_6H_5$.

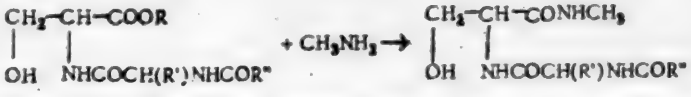
For the purpose of studying this phenomenon with derivatives of β-hydroxamino acids, a series of esters, amides and acylated peptides of serine were synthesized.

The synthesis was effected by reaction between hydrochlorides of serine esters and chlorides of acylated amino acids in conditions slightly departing from those given in the literature. Experiments were performed in presence of tertiary amines, which greatly simplified the course of the reaction and improved the yield of peptides [3].



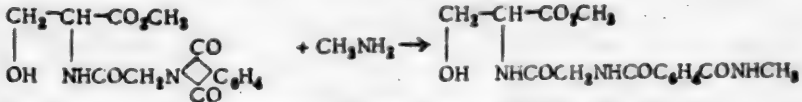
The following were synthesized: isopropyl ester of N-(phthaloylglycyl)-serine in 72% yield; methyl ester of N-(phthaloylglycyl)-serine in 54% yield; methyl ester of N-(benzoylphenylalanyl)-serine in 71% yield. The last-named was obtained in the form of two diastereoisomers.

In presence of methylamine, the methyl esters were transformed into the corresponding amides of N-acyl derivatives of peptides of serine



The following were synthesized: methylamide of N-(p-toluenesulfoglycyl)-serine in 75% yield and the methylamide of N-(benzoylphenylalanyl)-serine in abom 100% yield.

In the reaction of the methyl ester of N-(phthaloylglycyl)-serine with methylamine, the dimethylamide of N-phthaloylglycylserine was isolated instead of the anticipated amide



All the above-mentioned compounds are now prepared for the first time.

EXPERIMENTAL

1. Preparation of isopropyl ester of N-(phthaloylglycyl)-serine. To a solution of 1.12 g phthaloylglycyl chloride in 5 ml dioxane was added 0.92 g of the hydrochloride of the isopropyl ester of serine and (gradually) 2 ml diethylaniline (the solution being cooled from time to time). Mixing resulted in rapid solution with appreciable heat generation. Crystals rapidly separated and after 20-25 minutes the reaction mixture was very viscous. After an interval of 50 minutes from the start of the reaction, addition was made of 15 ml ligroine. The reaction mixture formed two layers which after energetic shaking for an hour changed into a thick, crystalline mass. After filtration and washing on the filter first with ligroine and then with water, the substance was recrystallized from chloroform (a mixture of dichloroethane and ligroine could also be used) to give 1.27 g isopropyl ester of N-(phthaloylglycyl)-serine. Yield 72%, m.p. 187°.

Found %: N 8.58, 8.56. $C_{16}H_{18}O_6N_2$. Calculated %: N 8.38.

2. Preparation of methyl ester of N-(phthaloylglycyl)-serine. To a solution of 8.94 g phthaloylglycyl chloride in 20 ml dioxane was added 8.24 g hydrochloride of the methyl ester of serine (m.p. 134°). To the resultant suspension was added in the course of 10 minutes, with cooling with cold water, 12 g diethylaniline dissolved in 10 ml dioxane. This caused nearly complete solution of the precipitate, followed after 15 minutes by separation of the methyl ester of N-(phthaloylglycyl)-serine. After an hour the reaction mass solidified. The dioxane was driven off in vacuum, the residue worked up with water, filtered and recrystallized from alcohol.

Yield 6.7 g methyl ester of N-(phthaloylglycyl)-serine or 54% of the theoretical.

Found %: N 9.20. $C_{14}H_{14}O_6N_2$. Calculated %: N 9.15.

Since the esters of the serine derivatives crystallize badly and are, therefore, difficult to purify, the prepared compounds were utilized in the subsequent ammonolysis reaction without further purification or further investigation.

Reaction of methyl ester of N-(phthaloylglycyl)-serine with methylamine. To 3.09 g methyl ester of N-(phthaloylglycyl)-serine was added 5 ml of 33% solution of methylamine in methyl alcohol, rapid solution being observed. The reaction mass was kept at room temperature for 48 hours. A small quantity of crystals came down and was redissolved by gentle heating. The excess of methylamine and methyl alcohol was driven off in vacuum and the residual crystalline mass dissolved in alcohol. Addition of ether to the alcoholic solution brought down 0.95 g substance with m.p. 160°, readily soluble in water and alcohol, insoluble in ether and acetone.

Judging by the analysis the prepared compound was the dimethylamide of phthaloylglycylserine.

Found %: C 53.74, 53.72; H 6.07, 6.13; N 16.93, 16.89. $C_{15}H_{17}O_5N_3$. Calculated %: C 53.67; H 5.95; N 16.66.

Methyl ester of N-(p-toluenesulfoglycyl)-serine.

a) 4.7 g N-(p-toluenesulfo)-glycine (m.p. 145-146°), 4.5 g phosphorus pentachloride and 20 ml dichloroethane were stirred for an hour at room temperature; much hydrogen chloride was evolved. After complete solution, addition was made to the reaction mixture of 20 ml toluene. A gelatinous precipitate came down and was filtered. The filtrate was evaporated in vacuum at 30° and the precipitate was triturated with ligroine and transferred to a filter. It was N-(p-toluenesulfo)-glycyl chloride. Yield 3.2 g (63.0%). M.p. 85°. The substance was used without further purification.

b) To a mixture of 2.02 g of the hydrochloride of the methyl ester of serine (m.p. 134°) and a solution of 3.2 g N-(p-toluenesulfo)-glycyl chloride in 20 ml dichloroethane was gradually added, with stirring, 6 ml diethylaniline. With considerable heat development the hydrochloride of the serine methyl ester dissolved. After standing for an hour at room temperature, the whole mass thickened up considerably, owing to separation of crystals. 20 ml ligroine and 25 ml water were added: two transparent layers were formed. Shaking for an hour led to crystallization. The crystals were filtered, washed with ether and dissolved in butyl alcohol by heating. The insoluble portion was rejected and the filtrate was worked up with ether. The resultant crystals were filtered and washed with ether.

There was obtained 2 g methyl ester of N-(p-toluenesulfoglycyl)-serine. Yield 46% of the theoretical, m.p. 148-149°. The methyl ester of N-(p-toluenesulfoglycyl)-serine is soluble on heating in ethyl alcohol, dichloroethane and water, on cooling it comes down in the form of small needles. From aqueous solution it comes down in the form of an oil which slowly crystallizes. The compound was used for ammonolysis without further examination or purification.

Found %: N 8.49, 8.51, $C_{12}H_{16}O_6N_2S$. Calculated %: N 8.48.

Methylamide of N-(p-toluenesulfoglycyl)-serine. To 2 g methyl ester of N-(p-toluenesulfoglycyl)-serine was added 20 ml of 33% solution of methylamine in methyl alcohol. After 48 hours at room temperature, the methyl alcohol and the methylamine were distilled off in vacuum. The oily residue crystallized when triturated with a mixture of acetone and ether (1:1). The methylamide of N-(p-toluenesulfoglycyl)-serine was recrystallized from water. Yield 1.5 g (75%), m.p. 145°. It crystallizes from water in tablets. Soluble in methyl and ethyl alcohols, insoluble in ether.

Found %: C 47.68, 47.93; H 5.92, 6.01; N 12.8, 12.9; S 10.40, 10.35. $C_{12}H_{15}O_5N_3S$. Calculated %: C 47.41; H 5.77; N 12.76; S 9.72.

Methyl ester of N-(benzoylphenylalanyl)-serine. 2-Phenyl-4-benzyl-5-oxazolone, prepared by Mohr's method from 5.4 g benzoylphenylalanine, was dissolved in 15 ml dichloroethane and the resultant solution was gradually added to a solution of 3.12 g hydrochloride of serine methyl ester and 3.46 ml dimethylbutylamine in 15 ml dichloroethane. The reaction mixture was stirred for an hour. Solution was complete after 30 minutes. The solution was shaken with 20 ml water, then with 10 ml N-hydrochloric acid and again with 10 ml water. After drying over sodium sulfate, the dichloroethane was driven off in vacuum. The residue was a thick, resinous mass which was dissolved in alcohol and treated with 10 ml water. On shaking the heterogeneous mixture and cooling to 0°, crystals came down. These were filtered and washed 3 times with ether. There was obtained 3.2 g methyl ester of N-(benzoylphenylalanyl)-serine (preparation A). Yield 43% of the theoretical. M.p. 158-159°.

Found %: C 65.48, 65.51; H 6.18, 6.27; N 7.52, 7.66. $C_{19}H_{22}O_5N_2$. Calculated %: C 64.85; H 5.90; N 7.56.

From the mother liquor remaining after separation of the methyl ester of N-(benzoylphenylalanyl)-serine was obtained yet another substance (preparation B) by treatment with ligroine. Yield 28% of the theoretical. M.p. 138-140° (from benzene). A mixed test with the methyl ester of N-(benzoylphenylalanyl)-serine (A) gives a m.p. depression of 15°. The compound was evidently the diastereoisomer of preparation A, since on treatment with methylamine it is transformed into the methylamide of N-(benzoylphenylalanyl)-serine.

Methylamide of N-(benzoylphenylalanyl)-serine.

a) From methyl ester of N-(benzoylphenylalanyl)-serine with m.p. 158-159° To 2 g methyl ester of N-(benzoylphenylalanyl)-serine was added a tenfold excess of 33% solution of methylamine in methyl alcohol, and the solution was left 24 hours at room temperature. Part of the formed methylamide crystallized out. After inspissation of the mother liquor, the remainder separated.

On recrystallization from 50% aqueous alcohol, the methylamide of N-(benzoylphenylalanyl)-serine separates in the form of lustrous tablets soluble in hot ethyl and butyl alcohols and sparingly soluble in hot water. Yield of methylamide (A') nearly quantitative. M.p. 210°.

Found %: C 65.39, 65.35; H 6.38, 6.38; N 11.39, 11.40. $C_{20}H_{23}O_4N_3$. Calculated %: C 65.04; H 6.24; N 11.38.

b) From methyl ester of N-(benzoylphenylalanyl)-serine with m.p. 138-140°. The mother liquor remaining after separation of the methyl ester with m.p. 158-159° (A) was used for preparation of the amide. Evaporation of the mother liquor in vacuum left a viscous oil which was worked up with a tenfold excess of 33% solution of methylamine in methyl alcohol in which the oil dissolved completely. After 24 hours, the reaction mass set, owing to separation of crystals. These were filtered and recrystallized from a mixture of ethyl alcohol and acetic acid. The methylamide of N-(benzoylphenylalanyl)-serine (preparation B') forms acicular crystals. M.p. 230°.

Found %: C 65.43, 65.28; H 6.44, 6.42; N 11.4, 11.0. $C_{20}H_{23}O_4N_3$. Calculated %: C 65.04; H 6.24; N 11.38.

SUMMARY

The synthesis of a series of derivatives of serine peptides is described.

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FURAN COMPOUNDS

V. PREPARATION AND PROPERTIES OF 3-(2'-METHYL-5'-FURYL)-PROPEN-2-AL AND SOME OTHER DERIVATIVES OF 5-METHYL-2-FURALDEHYDE

A. A. Ponomarev and M. D. Lipanova

The condensation of 2-furaldehyde with various aldehydes and ketones has been the subject of numerous investigations. This route has served, in particular, for the synthesis of many unsaturated furanic aldehydes: furylacrolein its homologs, furylpentadienal, etc.; these investigations have been adequately reviewed in a series of papers [1, 2]. Of the unsaturated aldehydes of the furan series the most accessible and the one of greatest practical importance was furylacrolein, whose preparation and properties have been studied by many authors. M. V. Likhosherstov and co-workers [1] developed a novel method of synthesis of furylacrolein in a yield of up to 85%. These authors also closely investigated the reduction of furylacrolein with aluminum ethylate and established that in certain conditions the yield of furylallyl alcohol may reach 60-70%.

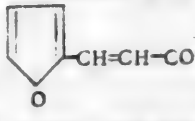
5-Methyl-2-furaldehyde has received very much less attention from investigators than 2-furaldehyde. This is also true in respect of such simple derivatives as unsaturated aldehydes and ketones. In the present paper we report the preparation and properties of some new derivatives of 5-methyl-2-furaldehyde. We have already [3, 4] described the synthesis of 3-(2'-methyl-5'-furyl)-propen-2-al from 5-methyl-2-furaldehyde and acetaldehyde. For its preparation we utilized at the time conditions similar to those adopted by M. V. Likhosherstov [1] for the synthesis of furylacrolein, i.e. condensation was effected with gradual addition of the acetaldehyde to a mixture, cooled to 0°, of 5-methyl-2-furaldehyde and a 0.5% solution of sodium hydroxide. The yield of 3-(2'-methyl-5-furyl)-propen-2-al was only 28% of the theoretical. Repeated experiments with maintenance of the specified conditions gave the same results.

In a further systematic study of this reaction it has been found that 3-(2'-methyl-5'-furyl)-propen-2-al is formed in considerably more satisfactory yield (67% of the theoretical) if the method is slightly modified so that the acetaldehyde (in slight excess) is added gradually to a mixture, kept at 20°, of 5-methyl-2-furaldehyde and 10% aqueous NaOH.

The 3-(2'-methyl-5'-furyl)-propen-2-al was further converted (in a yield of 27% of the theoretical) into 3-(2'-methyl-5'-furyl)-propen-2-ol-1 (methylfurylallyl alcohol) by reduction with aluminum ethylate in conditions similar to those for the preparation of furylallyl alcohol from furylacrolein [1]. The acetate of 3-(2'-methyl-5'-furyl)-propen-2-ol was also prepared.

It is a matter of some interest to compare the physical properties of furylacrolein and furylallyl alcohol and their methyl homologs.

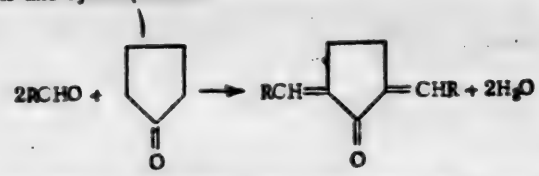
In Table 1 are set forth the data for all the above-mentioned substances.

We see from this table that furylacrolein and its methyl homologs are characterized by a EM_D of the order of 5 units, which is in full accord with the observation by a number of other authors [5, 6] of a considerable exaltation (4.1 to 5.8) in the case of furfurylidene ketones of the type of 

A similar phenomenon also occurs in other cases of conjugation of the double bond in the side chain with the furan ring and carbonyl (e.g. ethyl furylacrylate [7] has EM_D + 4.481); it is interesting to note that the exaltation is much lower when only a double bond in the side chain is conjugated with the furan ring, for instance, in furylethylene [7] EM_D 1.63, i.e., nearly the same as in 2-furaldehyde (1.61). As would also be expected in the light of the foregoing remarks, the molecular exaltations of furylallyl alcohols proved to be considerably lower than those of the

corresponding alcohols; in absolute magnitude they are close to the exaltation of furylethylene.

In Table 2 are set forth the data for some physical properties and color reactions of furanic unsaturated ketones which we prepared by condensation of 5-methyl-2-furaldehyde and 3-(2'-methyl-5'-furyl)-propen-2-al with cyclopentanone and cyclohexanone:



.. ketones possess a symmetrical structure and are formed in accordance with the above scheme.

close similarity between the above-enumerated ketones and the corresponding derivatives of 2-furaldehyde and furylacrolein is noteworthy.

EXPERIMENTAL

5-Methyl-2-furaldehyde was prepared from saccharose [11] as an oily liquid with b.p. 75-76° at 12 mm. Yield 22%.

Found %: C 65.81; H 5.93. $C_6H_6O_2$. Calculated %: C 65.45; H 5.50.

3-(2'-Methyl-5'-furyl)-propen-2-al. 450 ml 10% aqueous sodium hydroxide is mixed with 50 g 5-methyl-2-furaldehyde and a solution of 30 g acetaldehyde in 150 ml water is slowly stirred in at room temperature over a period of 2 1/2 hours. After all has been added, the mixture is stirred for another hour. The light-brown oil which separates at the bottom of the flask is collected; the aqueous layer is neutralized with 80% acetic acid and extracted 3 times with ether. The ethereal extracts are added to the oil and the ethereal solution is dried with calcined sodium sulfate. The ether is driven off and the residue distilled in vacuum at 5 mm. A fraction with b.p. 98-130° is collected and subjected to a second distillation. Methylfurylacrolein comes over at 100-102° (5 mm). Yield 41.5 g (67.13% of theoretical).

n_D^{20} 1.6089; d_4^{20} 1.1006; MR_D 42.82; Calc. 37.197.

Found %: C 70.53; 70.19; H 5.99, 5.69; M 134.1. $C_8H_8O_2$. Calculated %: C 70.57; H 5.92; M 136.14.

3-(2'-Methyl-5'-furyl)-propen-2-al is a yellow oil with an odor resembling that of furylacrolein but less pungent; it has a sweet taste; it is soluble in the common organic solvents, slightly soluble in water; darkens on keeping.

The semicarbazone is prepared by mixing an alcoholic solution of the aldehyde with a solution of semicarbazide hydrochloride and sodium acetate and directly heating the reaction mixture. Forms beautiful white scales. The yield is quantitative. M.p. 191° (after 3 recrystallizations from alcohol).

Found %: N 21.51, 21.35; $C_9H_{11}O_2N_3$. Calculated %: N 21.74.

The dinitrophenylhydrazone, prepared by the usual method, forms red crystals with m.p. 216-216.5° (after 3 recrystallizations from a mixture of alcohol and ethyl acetate).

3-(2'-Methyl-5'-furyl) propen-2-ol-1. Into a round-bottomed flask, fitted with a Hahn column, were introduced 30 g 3-(2'-methyl 5'-furyl)-propen-2-al, 150 ml dry benzene and 27 g aluminum ethylate; heating was carried out on a water bath until the benzene boiled, while passing a weak stream of nitrogen. The experiment lasted 2 1/2 hours. At the end of the experiment the solution had darkened appreciably. The benzene solution was then run in small portions into cooled 10% sulfuric acid whose amount was calculated for complete binding of the aluminum (245 ml). The benzene solution was separated and the aqueous portion further extracted with two portions (50 ml) benzene. The combined benzene extracts were washed with a small quantity of sodium carbonate solution and then with water and dried with calcined sodium sulfate. After driving off the solvent, the residue was distilled in vacuum and a first broad fraction (120-140° at 6 mm) collected. A second distillation of this fraction in vacuum (from a flask with a column) gave 8 g (27% of the theoretical) of 3-(2'-methyl-5'-furyl)-propen-2-ol with b.p. 125° (15 mm).

n_D^{20} 1.5561; d_4^{20} 1.088; MR_D 40.83; Calc. 38.71.

Found %: C 69.61, 69.81; H 6.85, 6.86; OH 10.55, 10.51. $C_8H_{10}O_2$. Calculated %: C 69.54; H 7.29; OH 12.3

TABLE 1

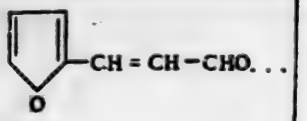
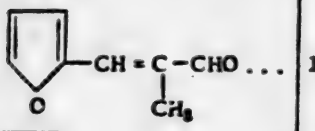
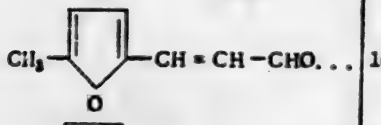
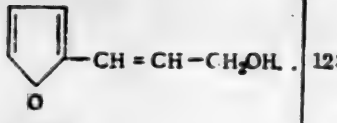
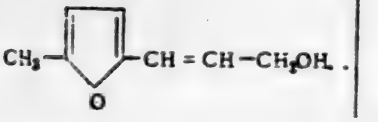
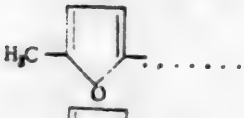
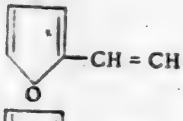
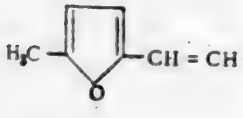
Structural formula	B.p. (°C)	d_4^t	n_D^t	MR_D found	MR_D calculated	M.p. of semicarbazone	Literature
	97 (10 mm)	1.1163 (at m.p.)	1.617 (at m.p.)	38.28	32.579	219	[5, 12]
	100 (11 mm)	1.1022 (13.5°)	1.613 (13.5°)	42.99	37.197	250.5-251.5	[5]
	100-102 (5 mm)	1.1066 (20°)	1.6089 (20°)	42.82	37.197	191	–
	123-124 (20 mm)	1.1001 (17.5°)	1.5514 (17.5°)	35.98	34.09	–	[1]
	125 (15 mm)	1.088 (20°)	1.5561 (20°)	40.83	38.71	–	–

TABLE 2

R	R–CH=(O)=CH–R				R–CH=(O)=CH–R			
	Color	M.p. (°C)	Color reactions* Conc. H_2SO_4	Color reactions* $SbCl_3$ and $CHCl_3$	Color	M.p. (°C)	Color reactions* Conc. H_2SO_4	Color reactions* $SbCl_3$ and $CHCl_3$
	Yellow	162-163 [8]	Dark-blue	Yellow, changing to green	Lemon-yellow	145 [9]	Violet	Yellow changing to green
	Yellow	131-132	Dark-blue	Green, changing to blue	Lemon-yellow	118-119	Violet	Green, changing to dark-blue
	Orange	151-152 [10]	Blue-green	Blue	Yellowish orange	162.4 [10]	Bluish-green	Blue
	Cherry red	165-166	Blue-green	Blue	Orange	168-168.5 [4]	Bluish-green	Blue

*The color developed bn adding particles of the substance to concentrated sulfuric acid, or on putting on filter paper drops of 1% solution of $SbCl_3$ in chloroform containing a particle of the substance.

The alcohol is a yellowish oil with a pleasant odor, soluble in the common organic solvents, slightly soluble in water. It polymerizes relatively quickly when kept.

The acetate is prepared by heating a mixture of 4.4 g acetic anhydride, 1 g fused sodium acetate and 4 g methylfuryiallyl alcohol for an hour on a water bath. The reaction mixture is washed with water, then with sodium carbonate solution, and extracted with ether. The extract is dried with calcined sodium sulfate, the ether is driven off and the residual oil distilled in vacuum. A fraction (1.28 g) with b.p. 107-109° (5 mm) is collected. Greenish-yellow liquid with a pleasant odor.

n_D^{20} 1.5221; d_4^{20} 1.0736; MR_D 51.2; Calc. 48.07.

Found %: C 66.72; H 6.80. $C_{10}H_{12}O_3$. Calculated %: C 66.65; H 6.71.

The phenylurethane was prepared by mixing equimolar amounts of the alcohol and phenylisocyanate and heating the mixture. White crystals. After 3 recrystallizations from carbon tetrachloride, needles with m.p. 106°.

Found %: N 5.7. $C_{17}H_{17}NO_3$. Calculated %: N 5.57.

Condensation of 5-methyl-2-furaldehyde with cyclopentanone. To a solution of 5 g 5-methyl-2-furaldehyde (0.0454 mole) and 1.9 g cyclopentanone (0.0227 mole) in 20 ml 60% alcohol was added dropwise 0.5 ml 10% NaOH solution. Heat was developed and after a short interval a voluminous orange precipitate had formed. The crystals were separated and washed with water and dilute alcohol. Yield of unpurified material 5.6 g (m.p. 128-129°). After two recrystallizations from alcohol, yellow acicular crystals were obtained with monoclinic syngony and slight pleochroism. M.p. 131-132°.

Found %: C 75.94, 76.36; H 6.47, 5.86; M 250.4 (Rast). $C_{19}H_{18}O_3$. Calculated %: C 76.10; H 6.01; M 263.29.

The ketone is poorly soluble in cold alcohol and benzene; readily soluble in hot alcohol, chloroform, dioxane.

Condensation of 5-methyl-2-furaldehyde with cyclohexanone. To a solution of 5 g 5-methyl-2-furaldehyde (0.0454 mole) and 1 ml 10% NaOH solution in 20 ml 60% alcohol is gradually added a solution of 2.22 g cyclohexanone (0.0227 mole) in 5 ml alcohol. Heat is developed and the mixture turns cloudy; after a short interval a crystalline precipitate appears. This is collected and washed with water and dilute acetic acid. Weight of unpurified product 6.5 g. After two recrystallizations from alcohol, it forms lemon-yellow needles with m.p. 118-119°. Under the microscope it has the form of elongated, canary-yellow, hexagonal prisms which are strongly pleochroic.

Found %: C 76.84, 76.39; H 6.55, 6.69; M 2801 (Rast). $C_{21}H_{22}O_3$. Calculated %: C 76.57; H 6.43; M 282.3.

The ketone is insoluble in cold and hot water, sparingly soluble in cold alcohol and benzene; it is readily soluble in hot alcohol, chloroform and dioxane.

Condensation of 3-(2'-methyl-5'-furyl)-propen-2-al with cyclopentanone. To a solution of 2 g methylfurylacrolein (0.014 mole) and 0.61 g cyclopentanone (0.07 mole) in 10 ml 60% ethyl alcohol is added dropwise, with shaking, 0.5 ml 10% NaOH solution. After a few minutes a dark oil begins to form and quickly solidifies. The crystals are collected and worked up as previously. Yield of unpurified product, 2.35 g. After recrystallization from isopropyl alcohol, it forms cherry-red needles with m.p. 165-166°. Under the microscope it appears as slender, red prisms without pleochroism and with tetragonal syngony.

Found %: C 78.59, 78.86; H 6.84, 6.82; M 330.57, 329.51. $C_{21}H_{20}O_3$. Calculated %: C 78.72; H 6.31; M 320.37.

The ketone is insoluble in water, poorly soluble in cold alcohol, benzene, gasoline, and carbon tetrachloride; readily soluble in hot alcohol, benzene, chloroform.

Condensation of 3-(2'-methyl-5'-furyl)-propen-2-al with cyclohexanone. The experiment was performed as previously described [4]. To a solution of 6 g of the aldehyde (0.044 mole) and 1 ml 10% NaOH solution in 20 ml 60% alcohol is added dropwise a solution of 2.16 g cyclohexanone (0.022 mole) in 5 ml alcohol. The crystals formed are treated as before. The ketone $C_{21}H_{20}O_3$ forms orange crystals with m.p. 168-168.5°, appearing under the microscope as prismatic tablets, slightly pleochroic from light-orange to deep orange, and possibly possessing rhombic syngony. Insoluble in cold and hot water, poorly soluble in cold alcohol and benzene; readily soluble in hot alcohol, chloroform, dioxane.

SUMMARY

1. A method is developed for the preparation of 3-(2'-methyl-5'-furyl)-propen-2-al which permits the synthesis of this aldehyde in a yield up to 70%. It is shown that 3-(2'-methyl-5'-furyl)-propen-2-al can be reduced with

aluminum ethylate to give the unsaturated alcohol 3-(2'-methyl-5'-furyl)-propen-2-ol-1; the properties of the latter and some of its derivatives are described.

2. A description is given of some properties of unsaturated furanic ketones prepared by condensation of 5-methyl-2-furaldehyde and 3-(2'-methyl-5'-furyl)-propen-2-al with cyclopentanone and cyclohexanone.

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* See Consultants Bureau Translation, page 663.

** See Consultants Bureau Translation, page 1127.

*** See Consultants Bureau Translation, page 1493.

PREPARATION OF THIOPHENE AND ITS HOMOLOGS FROM ALCOHOLS

Yu. K. Yuryev and L. I. Khmelnitsky

According to the data of Conary and co-workers, thiophene and its homologs can be obtained by interaction of hydrocarbons with sulfur dioxide in presence of chromia-on-alumina (20% chromia) at 500-600° [1, 2, 3]. This reaction is applicable to hydrocarbons containing not less than four carbon atoms in a straight chain. Butane and butenes give thiophene in 32% yield (on the hydrocarbon used); hydrocarbons with five and six carbon atoms give the corresponding thiophene homologs in much lower yields, the reaction being complicated by processes of cleavage giving rise to lower homologs of thiophene and thiophene itself.

In this investigation we have studied the interaction of aliphatic alcohols (n-butyl, isoamyl and n-hexyl) with sulfur dioxide in presence of chromia-on-alumina (20% chromia). It was found that the unsaturated hydrocarbons resulting from dehydration of the alcohols can react with sulfur dioxide to give compounds of the thiophene series, and that the optimum conditions for this reaction are 400-450° and a molar ratio of SO_2 to alcoho. of 1,5 : 1.

An examination of the liquid and gaseous products of the reaction of n-butyl alcohol with sulfur dioxide in optimum conditions showed that 8-10% of the alcohol is converted (after dehydration) into thiophene, approximately 6% only undergoes dehydration to 1-butene (isomerizing further to 2-butene and partly dehydrogenating to 1,3-butadiene), and approximately 24% of the alcohol is oxidized to butyraldehyde which breaks down to carbon monoxide and propane; the latter dehydrogenates to propene

$$CH_3CH_2CH_2CH_2OH \xrightarrow{-H_2} CH_3CH_2CH_2C\overset{O}{\underset{H}{<}} \xrightarrow{-CO} CH_3CH_2CH_3 \xrightarrow{-H_2} CH_3CH=CH_2$$

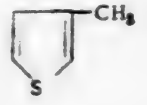
The remaining (approximately 60%) n-butyl alcohol undergoes more drastic oxidation with formation of carbon monoxide and a carbonaceous mass deposited as a dense layer on the catalyst. Less than 1% of the alcohol is recovered unchanged.

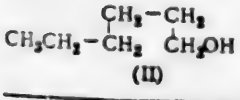
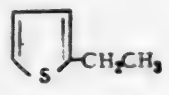
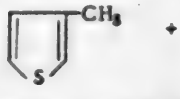
When the n-butyl alcohol is passed over the same catalyst at 450° in the absence of sulfur dioxide, dehydration proceeds normally (to the extent of 95%) with formation of 1-butene which isomerizes to the extent of 80-85% to 2-butene [4] (the percent isomerization was determined by examination of the Raman spectra of the mixture of dibromobutanes formed).

If the alcohol is first dehydrated and then the moist mixture of butenes is brought into reaction with sulfur dioxide at 550°, then thiophene is obtained in 33% yield (calculated on the alcohol).

In the interaction of isoamyl and n-hexyl* alcohols with sulfur dioxide, the formation would be expected of 3-methylthiophene and 1-ethylthiophene or 2,5-dimethylthiophene respectively, or of a mixture of both.

It was found that isoamyl (I) gave, together with 3-methylthiophenol, an insignificant amount of thiophene itself; in the case of n-hexyl alcohol (II), however, the product was 2-ethylthiophene, together with 3-methylthiophene and thiophene, whereas 2,5-dimethylthiophene was not formed at all.

(I) $CH_3-CH(CH_3)-CH_2-CH_2OH + SO_2 \xrightarrow{Cr_2O_3/Al_2O_3}$  + 

 $+ SO_2 \xrightarrow{Cr_2O_3/Al_2O_3}$  +  + 

(II)

*Catalytic dehydration of n-hexyl alcohol at 450° gave a mixture of isomeric hexenes in a yield of 80%.

EXPERIMENTAL

Chromia-on-alumina was prepared by the known method [5]: mixing of a chromic solution with non-calcined aluminum oxide. The catalyst was dried first at 110° and then in a current of air at an elevated temperature up to 450°. The activity of the catalyst was checked by the preparation of thiophene from a mixture of butenes and sulfur dioxide at 550°; the thiophene yield was 25.7% of the theoretical (the literature [1] reports 27.2%). The activity did not diminish after a large number of experiments.

Before each experiment the reaction tube was heated to 550° and the catalyst was activated for 2-3 hours* in an air current after which the operating temperature was established. The sulfur dioxide was passed through a flowmeter, a bubble counter containing sulfuric acid, and entered the reaction tube; the alcohol was run in from a dropping funnel.

1) Thiophene from n-Butyl Alcohol

a) First series of experiments: 35 g (50 ml) catalyst; tube with inner diameter of 13 mm. In each experiment, 25 g (0.34 mole) n-butyl alcohol (b.p. 115-116° at 751 mm; n_D^{20} 1.3981; d_4^{20} 0.8101) was introduced in a stream of sulfur dioxide. Experiments were run at 375, 400, 450, 500 and 550° and SO_2/alcohol molar ratios of 0.6:1 to 3.2:1. The space velocity of the alcohol was varied from 0.1 to 0.5 ml alcohol per ml catalyst per hour.

The reaction tube was connected to two receivers cooled with ice and salt; the main bulk of catalyzate collected in the first receiver. Suspended sulfur hindered the separation of the aqueous layer from the dark, oily layer; the catalyzate was therefore saturated with caustic alkali and extracted with ether. The ethereal extract was dried with fused NaOH and the residue distilled from a flask through a tall and narrow column.

Results of some experiments in this series are set forth in Table 1.

TABLE 1

No. of Experiment	Temperature (°C)	Space velocity of alcohol: ml alcohol/ml catalyst · hour	Velocity of SO_2 ml/min	Molar ratio of SO_2 to alcohol	Wt. of catalyst (g)	Thiophene obtained			Alcohol recovered unchanged		
						(g)	in % theory	b.p. (°C)	(in g)	in % of theory	b.p. (°C)
1	375	0.19	56	1.3	22	1.3	4.6	84-87	1.6	6.4	112-117
6	400	0.10	34	1.5	13	2.5	8.8	84-87	0.35	1.4	113-116
14	450	0.16	56	1.5	16	2.6	9.2	83-86	–	–	–
28	500	0.49	135	1.2	10	0.9	3.2	84-85	–	–	–
26	550	0.44	135	1.4	10	0.75	2.7	83-84	–	–	–

In experiment 14 (Table 1) distillation of the reaction product (obtained at 450°) gave a fraction with b.p. 83-86° (746 mm), 2.6 g (residue 0.2 g) consisting of thiophene (yield 9.2% of the theoretical).

Repeated distillation of the thiophene (24.7 g) from all the experiments over sodium gave pure thiophene (23.5 g): b.p. 83-84° (751 mm); n_D^{20} 1.5250; d_4^{20} 1.0618; MR_D 24.28. C_4H_4S. Calculated: MR_D 25.34.

Found %: S 38.10, 38.04. C_4H_4S. Calculated %: S 37.93.

Mercuration [6] of the thiophene gave 2-chloromercurithiophene with m.p. 183-184°.

Found %: Hg 62.91, 62.96. C_4H_3HgCl. Calculated %: Hg 62.85.

Literature data for thiophene [7]: b.p. 84° (760 mm); n_D^{20} 1.5246; d_4^{20} 1.0617; [8]: b.p. 84.12° (760 mm); n_D^{20} 1.5287; d_4^{20} 1.0644. M.p. of 2-chloromercurithiophene [1]: 183-184°.

b) Second series of experiments: amount of catalyst 71 g (100 ml) and 104 g (150 ml), tube with internal diameter 20 mm. At 450°, from 50 to 100 g n-butyl alcohol was reacted with a space velocity of 0.5-1.4 with a SO_2/alcohol ratio of 1.5 : 1.

It was found that the increased space velocity of the alcohol had no effect on the thiophene yield. Thus, for instance, distillation of the product of reaction from 76.5 g alcohol (100 ml catalyst, space velocity of introduction of alcohol 1.3) gave the following fractions: 1) b.p. 84-87° (742 mm), 9.1 g; 2) b.p. 87-112°, 0.3 g;

*More prolonged activation (up to 7 hours) did not improve the yield of thiophene.

3) b.p. 112-116°, 0.7 g. The first fraction was thiophene (yield 10.5%), the third fraction was unchanged alcohol.

The gaseous products of reaction (79.0 g alcohol, 100 ml catalyst, space velocity of introduction of alcohol 0.72) were purified from hydrogen sulfide, sulfur dioxide, and (partly) carbon dioxide and collected in a gasholder. Gas composition (27 liters at N.T.P.): CO_2 8.1%; CO 20.5%; H_2 36.2%; O_2 2.4%; C_nH_{2n} 20.2%; C_nH_{2n+2} 12.2%.

c) Third series of experiments: into a furnace were introduced two tubes with inner diameter, 18 mm: the first contained 80 g (140 ml) alumina, the second 80 g (115 ml) chromia-on-alumina. Into the first tube, in a weak nitrogen stream, was introduced 71 g alcohol with a space velocity of 0.5, and the mixture of butenes formed was, without drying, passed into the second tube into which was introduced sulfur dioxide at a velocity of 360 ml/min. Molar ratio of SO_2 to alcohol 1.5 : 1. The catalyzate was saturated with alkali and thrice extracted with ether. The ethereal extract was dried with NaOH, the ether was driven off, and the residue distilled to give 26.5 g thiophene which came over at 83-84° (750 mm) (yield 33% calculated on the alcohol brought into the reaction).

d) Reaction between n-butyl alcohol and sulfur dioxide was carried out in presence of alumina alone. into a tube with an inner diameter of 13 mm was charged 35 g (75 ml) alumina and at 450°, 25 g (0.34 mole) n-butyl alcohol was passed in at a space velocity of 0.3; speed of introduction of sulfur dioxide 100 ml/min. (molar ratio of SO_2 to alcohol 1.5 : 1). The thiophene yield was 1.6 g (5.8% of the theoretical).

2) 3-Methylthiophene from Isoamyl Alcohol

a) First series of experiments: 35 g (50 ml) catalyst; tube with inner diameter of 13 mm. In each experiment was introduced 25.5 g (0.29 mole) isoamyl alcohol [b.p. 128-130° (753 mm); n_D^{20} 1.4060; d_4^{20} 0.8129] in a stream of sulfur dioxide. Experiments were run at 400 and 450°, molar ratio of SO_2 to alcohol of 1.3:1 1.65:1, and space velocity of introduction of alcohol 0.30 to 0.63. The catalyzates were worked up as described above. Yields of 3-methylthiophene at 400 and 450° were substantially identical and reached 12.4%, reckoned on the alcohol used. Thus, for example, distillation of the product of reaction at 400°, molar ratio of SO_2 to alcohol of 1.6:1, and space velocity of introduction of the alcohol 0.30, gave the following fractions: 1) b.p. 84-110° (750 mm), 0.2 g; 2) b.p. 110-113°, 3.3 g; 3) b.p. 113-127°, 0.3 g; 4) b.p. 127-132°, 2.5 g; resinous residue, 0.8 g. The first fraction contained thiophene; the second fraction was 3-methylthiophene (yield 12.4% of theoretical, reckoned on the alcohol used); the fourth was unchanged alcohol.

Redistillation over sodium of the 3-methylthiophene (22 g) from all the experiments gave pure 3-methylthiophene (20.6 g): b.p. 114-115° (751 mm); n_D^{20} 1.5200; d_4^{20} 1.0207; MR_D 29.24. C_5H_6S. Calculated MR_D 29.96.

Found %: S 32.62, 32.52. C_5H_6S. Calculated %: S 32.67.

Literature data for 3-methylthiophene [9]: b.p. 115.4° (760 mm); n_D^{20} 1.5204; d_4^{20} 1.0216.

b) Second series of experiments: 100 ml catalyst; tube with inner diameter, 20 mm. In an experiment at 400° 91 g (1.04 moles) isoamyl alcohol (molar ratio of SO_2 to alcohol of 1.4:1, space velocity of alcohol 0.6) was passed over the catalyst. The catalyzate was worked up with alkali and the oily layer was collected and distilled (to eliminate resin) before drying with fused NaOH; it was then combined with the residue (usually not more than 0.7 g) obtained after driving off the ether (in vacuum) from the ethereal extract of the aqueous layer. Further distillation of the reaction product (from a flask with a tall and narrow column) gave the following fractions: 1) b.p. 83-84° (754 mm), 0.3 g; 2) b.p. 84-112°, 0.4 g; 3) b.p. 112-115°, 8.2 g; 4) b.p. 115-127°, 1.6 g; 5) b.p. 127-130°, 18.4 g; residue 0.8 g. The first fraction was thiophene (yield 0.4% reckoned on the alcohol used), the third was 3-methylthiophene (yield 10%), the fifth was unchanged alcohol (20.2%). In experiments at 450° (other conditions being identical) the yield of thiophene was 8%.

Hence, the increase of space velocity of introduction of the alcohol from 0.3 (first series) to 0.6 (second series) caused a reduction in 3-methylthiophene yield from 12.4 to 10% (at 400°) and to 8% (at 450°).

The corresponding fractions of thiophene from all the experiments of the second series were combined, distilled over sodium and fractionated through a column with an efficiency of 16 theoretical plates, the following fractions being obtained:

	B.p. (747 mm)	n_D^{20}	d_4^{20}	Wt. (in g)
1	70-84°	1.5094	—	0.8
2	84-86	1.5147	1.0326	1.0
3	86-112.5	1.5172	1.0271	3.2
4	112.5-113.5	1.5196	1.0226	4.2
5	113.5	1.5202	1.0217	11.2
6	113.5-119	1.5190	1.0207	1.5

TABLE 2

No. of Experiment	Hexyl alcohol charged (in g)	Space velocity of alcohol charged	Velocity of introduction of SO_2 (ml/min.)	Molar ratio of SO_2 to alcohol	Catalyzate obtained (in g)	B.p. and amount		
						1	2	3
						52-84°	84-92°	92-111°
1	102	0.75	575	1.5	104	19.6	0.8	1 drop
2	91	0.75	575	1.6	92			
3	102	0.34	260	1.5	99	91	0.2	0.1
4	102	0.52	575	2.2	88	5.4	0.4	1 drop

The fifth fraction was pure 3-methylthiophene which was also present in the fourth and fifth fractions.

The second fraction (judging by the boiling point) must be thiophene but the refractive index and density of this fraction were higher than those reported in the literature for thiophene; mercuration [10] was therefore effected of this fraction as well as of the first fraction.

A mixture of 0.6 g first fraction and 0.2 g second fraction gave 1.7 g 2-chloromercurithiophene with m.p. 183-184° (no depression was observed in a mixed test with pure 2-chloromercurithiophene) and 1 g 2,5-di-(chloromercuri)-thiophene; analysis of the latter gave the following results:

Found %: Hg 72.51, 72.59. $C_4H_2SHg_2Cl_2$. Calculated %: Hg 72.38.

Mercuration of 14 g of mixture of the fourth and fifth fractions gave 17.3 g 2-chloromercuri-3-methylthiophene with m.p. 128-129°.

Found %: Hg 60.25, 60.17. C_5H_5SHgCl. Calculated %: Hg 60.20.

There was also obtained 33.1 g 2,5-di-(chloromercuri)-3-methylthiophene.

Found %: Hg 70.34, 70.43. $C_5H_4SHg_2Cl_2$. Calculated %: Hg 70.59.

The literature for 2-chloromercuri-3-methylthiophene [1] gives m.p. 128-129°.

Heating of 2,5-di-(chloromercuri)-3-methylthiophene with 20% hydrochloric acid gave 4.4 g pure 3-methylthiophene: b.p. 115.1-115.4° (755 mm); n_D^{20} 1.5207; d_4^{20} 1.0203; MR_D 29.28. C_5H_6S. Calculated: MR_D 29.96.

Found %: S 32.59, 32.66. C_5H_6S. Calculated %: S 32.67.

A comparison of the constants of the two preparations of 3-methylthiophene (that obtained from the product of reaction by distillation in a column and that obtained from 2,5-di-(chloromercuri)-3-methylthiophene) indicates the high degree of purity of the first preperation.

3) 2-Ethylthiophene from n-Hexyl Alcohol

104 g (150 ml) catalyst; tube with inner diameter of 20 mm. The n-hexyl alcohol [b.p. 155-156° (757 mm); n_D^{20} 1.4210; d_4^{20} 0.8199] was introduced in a stream of sulfur dioxide at 450°. The first two experiments were run in identical conditions and their catalyzates were worked up together. The experimental conditions and the results of fractional distillations are set forth in Table 2.

The yield of 2-methylthiophene was calculated on the basis of the 4th fraction (reckoned on alcohol used) and that of 2-ethylthiophene on the basis of the 6th fraction; the 8th fraction was unchanged hexyl alcohol. The average yield of thiophene present in the first and second fractions was 2%; it was determined from the weight of the 2nd fraction and from the chloromercuri derivative of thiophene subsequently prepared from the first fraction.

The first fractions from all the four experiments were combined and distilled in a column with an efficiency of 40 theoretical plates, the following being isolated:

a) 12.9 g of a mixture of hexenes with b.p. 62.5-69.0° (742 mm).

Found %: C 85.60, 85.49; H 14.55, 15.51. C_6H_{12}. Calculated %: C 85.63; H 14.37.

b) 10.4 g with b.p. 78.5-81.0° (742 mm), mercuration of which gave 9.1 g 2,5-di-(chloromercuri)-thiophene and 12.2 g 2-chloromercurithiophene with m.p. 183-184° (no depression in mixed melting test with pure 2-chloromercurithiophene). Decomposition of the chloromercuri derivatives of thiophene with 20% hydrochloric acid gave 3.5 g pure thiophene b.p. 83.5-84° (754 mm); n_D^{20} 1.5246; d_4^{20} 1.0615; MR_D 24.27. C_4H_4S. Calculated: MR_D 25.34.

TABLE 2 (CONT.)

(in g) of fractions of catalyzate						Yields (%)		
4	5	6	7	8	residue	2-methylthiophene (4th fraction)	2-ethylthiophene (6th fraction)	n-hexyl alcohol (8th fraction)
111-118°	118-130°	130-140°	140-151°	151-155°				
6.4	0.6	5.9	0.3	28.3	1.5	4	3.3	15.2
3.6	0.7	1.3	0.3	17.9	1.5	4.5	1.4	17.5
2.4	0.3	0.6	0.3	15.9	1.6	2.9	0.6	15.6

Fractions 2 to 7 from all the experiments were fractionated in a column with an efficiency of 25 theoretical plates to give the 8 fractions listed in the table below.

	B.p. 769 mm	n_D^{20}	d_4^{20}	Wt. (in g)
1	67-84°	1.4880	0.9813	2.1
2	84.0-112.5	1.5019	1.0012	1.9
3	112.5-113.4	1.5185	1.0139	7.6
4	113.4-115.5	1.5198	1.0142	3.2
5	115.5-134.1	1.5068	0 9805	1.8
6	134.1-134.5	1.5022	0.9696	0.9
7	134.5-136.5	1.5007	0.9682	3.5
8	136.5	1.5026	0.9684	1.4
	Residue	—	—	1.0

The first fraction contained thiophene; the third and fourth were 2-methylthiophene; the sixth, seventh, and eighth were 2-ethylthiophene.

Mercuration of 1.4 g of the first fraction gave 0.7 g 2-chloromercurithiophene with m.p. 183-184° (no depression observed in mixed test with authentic 2-chloromercurithiophene) and 2.4 g 2,5-di-(chloromercuri)-thiophene.

Found %: Hg 72.48, 72.59. $C_4H_2SHg_2Cl_2$. Calculated %: Hg 72.38.

From 8.4 g mixture of third and fourth fractions was obtained 23 g 5-chloromercuri-2-methylthiophene with m.p. 204.0-204.5°.

Found %: Hg 60.47, 60.39. C_5H_5SHgCl. Calculated %: Hg 60.20.

Heating of 21.5 g 5-chloromercuri-2-methylthiophene with 20% hydrochloric acid gave 5 g 2-methylthiophene with b.p. 112.3-112.5 (754 mm); n_D^{20} 1.5210; d_4^{20} 1.0202; MR_D 29.30. C_5H_8S. Calculated: MR_D 29.96.

Found %: S 32.50, 32.57. C_5H_8S. Calculated %: S 32.67.

Literature data for 2-methylthiophene [10]: b.p. 112.5° (760 mm); n_D^{20} 1.5203; d_4^{20} 1.0194; m.p. of 5-chloromercuri-2-methylthiophene [1] 204-205°.

3.8 g of mixture of seventh and eighth fractions gave 8.0 g 5-chloromercuri-2-ethylthiophene with m.p. 147-148°

Found %: Hg 57.76, 57.67. C_6H_7SHgCl. Calculated %: Hg 57.77.

Heating of 6.7 g 5-chloromercuri-2-ethylthiophene with 20% hydrochloric acid gave 0.92 g 2-ethylthiophene: b.p. 135.5-136.5° (758 mm); n_D^{20} 1.5137; d_4^{20} 0.9928; MR_D 34.00. C_6H_8S. Calculated: MR_D 34.57.

Found %: S 28.41, 28.50. C_6H_8S. Calculated %: S 28.58.

Literature data for 2-ethylthiophene [11]: b.p. 133.0-134.5°; n_D^{20} 1.5122; [12]: d_4^{20} 0.922; m.p. of 5-chloromercuri-2-ethylthiophene [1]: 146-147°.

SUMMARY

1. Interaction of n-butyl, isoamyl or n-hexyl alcohols with sulfur dioxide in presence of chromia-on-alumina leads to thiophene and its homologs respectively.

2. In optimum conditions the yield of thiophene from n-butyl alcohol reached 10%; the yield of 3-methylthiophene from isoamyl alcohol reached 12.4%; the yields of 2-ethylthiophene, 2-methylthiophene and thiophene

from n-hexyl alcohol were, respectively, 3.3, 4 and 2%.

3. In the preparation of thiophene by the action of sulfur dioxide on a wet mixture of the butenes formed by dehydration of n-butyl alcohol, the yield of thiophene was 33% (reckoned on the alcohol).

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UNSATURATED CYCLIC HYDROCARBONS AND THEIR HALOGEN DERIVATIVES

XIII. THE MECHANISM OF CONJUGATED HALOGENATION AND DEHALOGENATION

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In our previous communications [1, 2] it was shown that the transformation of 1,2-dibromocyclohexane into benzene by heating with quinoline actually takes place through the intermediate formation of 1,3-cyclohexadiene and of perbromides of quinoline (products of addition of bromine and hydrogen bromide to quinoline). These observations confirmed the first and second stages of the scheme that one of us [3] had proposed for transformation of polyhalo derivatives of cyclohexane into aromatic compounds when heated with quinoline.

We could have confirmed the third stage of the scheme if we had isolated 1,4-dibromocyclohexene-2 in the reaction of 1,2-dibromocyclohexane with quinoline. We failed to achieve this, however, both in this reaction and in the reaction of 1,3-cyclohexadiene with hexabromoethane and quinoline [1]. For the purpose of demonstrating the third stage of the proposed scheme, we carried out the reaction of 1,3-cyclohexadiene, in the absence of free quinoline, with a series of quinoline perbromides: quinoline hydrobromide dibromide, quinoline tetrabromide and quinoline dibromide; these compounds, in our opinion, could be formed in the conditions of conjugated halogenation and dehalogenation.

It was established that heating of 1,3-cyclohexadiene with quinoline hydrobromide dibromide gives exclusively tetrabromocyclohexane, while in the cold a mixture of dibromocyclohexene and tetrabromocyclohexane is obtained. In the cold with quinoline tetrabromide, a crystalline product is obtained which consists of a mixture of approximately equal parts of dibromocyclohexene and tetrabromocyclohexane. In the cold with quinoline dibromide, the product is dibromocyclohexene free from tetrabromocyclohexane.

The tetrabromocyclohexane is evidently 1,2,3,4-tetrabromocyclohexane. The dibromide is very probably 1,4-dibromocyclohexene-2 since systems containing conjugated double bonds possess a great tendency to undergo addition reactions in the 1,4-position. Moreover, the investigation of Farmer and Scott [5] have shown that 1,2-dibromocyclohexene-3 may be obtained by addition of bromine to 1,3-cyclohexadiene at $-15°$ and only with maintenance of a number of other conditions. The authors showed that it isomerizes very easily into 1,4-dibromocyclohexene-2 when heated and that this process even takes place spontaneously on keeping.

All our attempts to confirm the structure of the dibromocyclohexene prepared with quinoline dibromide have so far been unsuccessful. Ozonization of the bromide gave a very unstable ozonide. After complete removal of the solvent (chloroform) it spontaneously ignited. When the solvent is not completely eliminated, the ozonide is decomposed by water with great difficulty, and titration with alkali leads to formation of very glutinous, ropy films which appeared to consist of a polymeric product although it defied further examination. Oxidation with potassium permanganate solution at room temperature also failed to throw light on the structure of this dibromide. Oxidation was performed in presence of the calculated amount of potassium bisulfate in order to avoid the extremely undesirable alkaline reaction of the medium, since two bromine atoms (in 1,4-dibromocyclohexene-2) or one (in 1,2-dibromocyclohexene-3) in the dibromocyclohexene formed are allylic. Oxidation was accompanied by evolution of bromine which was clearly detected by the odor. Oxidation gave (apart from unchanged dibromocyclohexene) only succinic acid, which could have been formed either by oxidation of 1,4-dibromocyclohexene-2 or of 1,2-dibromocyclohexene-3.

Attention must be drawn to the fact that the attempts of a number of investigators to establish the structure of the dibromocyclohexene with m.p. 108°, and believed to be 1,4-dibromocyclohexene-2, have likewise not met with success [4, 5, 6, 18]. The work of Ziegler [16], however, makes it probable that in this dibromide the bromine atoms are in the 1,4-position and not in the 1,2-position.

In our latest investigation we studied the action of quinoline on the crystalline dibromides obtained by reaction of 1,3-cyclohexadiene with each of the quinoline perbromides in order to establish whether they are capable of transformation into aromatic compounds under the action of quinoline, i.e., in order to establish whether the bromides formed are indeed intermediate products during conjugated halogenation and dehalogenation, as should follow from the fourth stage of the scheme. With this objective, each of the above-noted crystalline products was heated with quinoline. The following facts emerged from a study of the ultraviolet absorption spectra: a) Quinoline reacts with the tetrabromocyclohexane obtained by heating 1,3-cyclohexadiene with quinoline hydrobromide dibromide to give a product containing about 90% bromobenzene, the action of quinoline on the crystalline product consisting mainly of dibromocyclohexene (obtained by reaction in the cold) gives nearly pure benzene; b) the product of interaction of 1,3-cyclohexadiene with quinoline tetrabromide reacts with quinoline in the cold to form a mixture of benzene and bromobenzene; c) treatment with quinoline of the crystals isolated on interaction of 1,3-cyclohexadiene with quinoline dibromide leads to a product containing about 90% benzene.

The formation of dibromocyclohexene by interaction of 1,3-cyclohexadiene with quinoline perbromides and the formation therefrom, by the action of quinoline, of benzene is evidence that dibromocyclohexene may indeed be an intermediate product in conjugated halogenation and dehalogenation. This is in accord with the third and fourth stages of the scheme which was advanced by one of us but which could not previously be confirmed.

EXPERIMENTAL

Reaction of 1,3-Cyclohexadiene with Quinoline Perbromides

Experiments were performed with cooling with iced water in a flask fitted with dropping funnel and reflux condenser. It should be noted that in the preparation of the dibromocyclohexene in which we are interested, it is more advantageous not to add the 1,3-cyclohexadiene dropwise to the quinoline perbromide (although this is more convenient) but to adopt the opposite procedure, even though experimentally less convenient: To the 1,3-cyclohexadiene (the amount varied from 3.5 to 8 g in different experiments) is added the quinoline perbromide in small portions through the reflux condenser. The smaller these portions the less is the product resinified and the smaller its content of tetrabromocyclohexane. With the reverse order of addition of the reactants, a mixture is formed of dibromocyclohexene and a fairly considerable amount of tetrabromocyclohexane. In all probability, this is because when 1,3-cyclohexadiene is added dropwise to quinoline perbromide, each drop of hydrocarbon comes into contact with a large quantity of quinoline perbromide which has a great tendency to release bromine atoms (exothermal reaction). This gives rise to local overheating which can facilitate both addition of four atoms of bromine to the 1,3-cyclohexadiene and excessive resinification.

1,3-Cyclohexadiene was prepared by a slight modification of the method of Hofmann and Damm [7]: instead of sodium ethylate we used a saturated solution of alcoholic alkali.

The quinoline required for preparation of quinoline perbromides was obtained by Skraup's synthesis.

1. Reaction of 1,3-cyclohexadiene with quinoline hydrobromide dibromide. Reaction with heating. Quinoline hydrobromide dibromide was prepared by a slight modification of the methods of Rosenmund [8] and Trowbridge [9]. 5 g quinoline was cooled in a round-bottomed flask; careful addition was made of 3.2 ml concentrated hydrochloric acid, the contents of the flask then crystallizing in the form of a snowy-white mass; gradual addition was then made of 42 ml iced water; the solution of quinoline hydrochloride was thoroughly cooled and 2.9 ml bromine was introduced. The pomegranate-red crystals of perbromide were filtered off, pressed and used for reactions without recrystallization.

6.2 g 1,3-cyclohexadiene was added in small portions to an equimolar amount of quinoline perbromide. The mixture was heated for 1-2 hours on an oil bath at 120-145°; the contents of the flask formed two opaque layers. The upper layer gave a very weak emulsion with water and an extremely minute amount of oil separated when treated with alkali solution. The lower layer was a brown-colored oily liquid much contaminated with resin; it was much heavier than water and not appreciably soluble in water. When washed with water (the wash liquor had an acidic reaction) it partly crystallized in the form of very hard crystals which after two recrystallizations from alcohol melted at 70-71.5°, weight 7.5 g (preparation I). Found: M 385.3, 378.6; % Br 80.23, 80.53. $C_6H_8Br_4$. Calculated: M 399.88; % Br 79.99.

For 1,2,3,4-tetrabromocyclohexane the literature data are: m.p. 87-89° [10], 87-88° [7, 12], 140-141° [10, 11], 90-92° [13], 155-156° [10], 184° [13, 14].

We see that the melting point of our crystals is lower than the lowest melting point reported in the literature

for the tetrabromides prepared from 1,3-cyclohexadiene. We evidently obtained one of the six possible stereoisomers of 1,2,3,4-tetrabromocyclohexane.

5 g 1,3-cyclohexadiene was added to an equimolar quantity of quinoline perbromide. The mixture was heated on an oil bath for 50 minutes at 100-110°. The lower layer was collected. Weight 11.1 g, brownish-black in color, did not form an emulsion with water; the wash liquor did not have an acid reaction. The unreacted hydrocarbon was drained off in vacuum, after which 4 g crystals separated from the oil. After three recrystallizations from alcohol they formed pinkish-yellow leaflets with m.p. 84.3-86.9°.

Found %: M 392.8, 404.8; % Br 80.25, 80.38. $C_6H_8Br_4$. Calculated: M 399.88; % Br 79.99.

Reaction in the cold. To 6.9 g 1,3-cyclohexadiene, cooled with iced water, was added through the reflux condenser 31 g quinoline perbromide in small portions. With progressive addition of the perbromide two layers formed in the flask; the nearly colorless upper layer had a quinoline odor, formed a weak emulsion with water, and did not give an acidic reaction; the lower layer (brown-red) did not give an emulsion with water and immediately settled to the bottom. Weight 20.3 g instead of 20.7 g calculated for the dibromocyclohexene formed. After standing for a short period the oil crystallized. The crystals were washed with alcohol. Recrystallization was not carried out to avoid loss of any components of the reaction mixture. Colorless, lachrymatory crystals (13.2 g) with m.p. 58-84° (preparation II).

Found: M 255.0, 265.5; % Br 69.45, 69.13. $C_6H_8Br_2$. Calculated: M 239.95; % Br 66.60.

The high bromine content found may be explained by the formation of higher bromo derivatives at the same time.

2. Interaction of 1,3-cyclohexadiene with quinoline tetrabromide in the cold. Quinoline tetrabromide was obtained in the form of a friable crystalline mass by Grimaux's method [15]: addition of 12 ml bromine, with cooling, to an emulsion of 15.2 g quinoline in 45 ml water; the product was utilized without recrystallization.

To 2.3 g 1,3-cyclohexadiene was added 13 g quinoline perbromide. Two layers formed in the flask. The upper one was nearly colorless, did not give an emulsion with water and had a neutral reaction; alkali solution brought down quinoline. The lower layer (8.9 g instead of the required 6.9 g of dibromocyclohexene) crystallized. After recrystallization from alcohol, the weakly lachrymatory, pinkish-yellow crystals melted at 60-88° (preparation III).

Found: M 315.3, 322.2; % Br 73.55, 73.90. $C_6H_8Br_2$. Calculated: M 239.95; % Br 66.60. $C_6H_8Br_4$. Calculated: M 399.88; % Br 79.99.

3. Interaction of 1,3-cyclohexadiene with quinoline dibromide in the cold. To a well-cooled emulsion of 12.5 g quinoline in 40 ml water was added, from a dropping funnel with very energetic stirring, 5.1 ml bromine. The orange-red crystalline mass was filtered off and pressed between sheets of filter paper (34 g instead of 28.5 g). The perbromide had m.p. 60-67°. Compare [19, 20, 21].

0.1696 g substance: 0.1992 g AgBr. 0.2049 g substance: 0.2412 g AgBr. Found %: Br 49.98, 50.10. $C_9H_7NBr_2$. Calculated %: Br 55.34.

The low percentage of bromine and the higher weight of perbromide than is required by the formula $C_9H_7NBr_2$ may be due to the same cause, namely addition of water to the quinoline dibromide molecule. Repeated observations led us to this conclusion. Thus, instead of 7 g quinoline dibromide we obtained 8.6 g; instead of 14 g we obtained 17.3 g, and so forth. Calculated: content of Br for $C_9H_7NBr_2 \cdot H_2O$ 52%; for $C_9H_7NBr_2 \cdot 2H_2O$ 49.2%.

After the reaction of quinoline dibromide with the unsaturated hydrocarbon, the water of hydration separates and collects in the form of a layer above the bromide formed from the hydrocarbon in the quinoline. The weight approximately corresponds to the observed excess over the theoretically calculated value for the preparation of quinoline dibromide.

To 7 g 1,3-cyclohexadiene was added with cooling, 25 g quinoline dibromide. The upper (colorless) layer weighed 12.2 g, did not give an emulsion with water and separated an insignificant amount of quinoline when treated with alkali. The lower layer (brown) weighed 20 g and crystallized. The crystals (repeatedly washed with alcohol) weighed 9.4 g; pink color, lachrymatory; m.p. 85-95° (preparation IV).

0.4530 g substance: 16.64 g benzene: Δt 0.574°. 0.3621 g substance; 16.64 g benzene: Δt 0.462°. 0.1920 g substance: 0.2993 g AgBr. 0.2003 g substance: 0.3130 g AgBr. Found: M 243.3, 241.6; % Br 66.34, 66.50. $C_6H_8Br_2$. Calculated: M 239.95; % Br 66.60.

The wide melting range of the crystals may be due to the formation in the given conditions of both of the possible 1,4-dibromocyclohexenes-2. We regard the formation of 1,2-dibromocyclohexene-3 in our reaction conditions to be very improbable in the light of the results of Farmer and Scott.

Action of Quinoline on the Bromides Obtained from 1,3-Cyclohexadiene and Quinoline Perbromides

4. Action of quinoline on the tetrabromide (I). 12 g tetrabromocyclohexane was very slowly and carefully heated in a Wurtz flask with 17 g quinoline until the first signs of start of reaction were observed; the heating was temporarily stopped at that point until the vigorous reaction had ceased. The distilled oil (3.4 g) was washed with dilute sulfuric acid and then with water and dried with calcium chloride before distillation. The fraction with b.p. 153-155° had d_4^{16} 1.5041 and n_D^{16} 1.5607.

The ultraviolet absorption spectrum showed that the product contained 90-95% bromobenzene.

5. Action of quinoline on bromide (II). 17.7 g crystals and 28 g quinoline were carefully heated until the first signs of reaction which afterwards proceeds very vigorously with evolution of much heat. The distillate (6.1 g) was washed with dilute sulfuric acid and water, dried with calcium chloride and metallic sodium and distilled.

The fraction with b.p. 79-82° (2.5 g) was a transparent liquid which crystallized below −8°; its constants were in fairly good agreement with those of benzene and the ultraviolet absorption spectrum indicated that it was about 90% benzene.

Bromine number by the McIlinnhey method [17] 1.0; $d_4^{17.5}$ 0.8848; $n_D^{17.5}$ 1.5023.

6. Action of quinoline on (III). To 8.1 g of the crystals obtained according to section 2 above was added 10 g quinoline. The mixture was cautiously heated until the reaction started. The distilled product was washed with dilute sulfuric acid and water and dried with calcium chloride. It boiled over the wide temperature range of 76-150° (1.95 g). The spectroscopic examination revealed a different absorption than for the 1,3-cyclohexadiene taken for reaction with quinoline tetrabromide; the absorption band has the fine structure characteristic of benzene but is blurred by its overlapping with the absorption of bromobenzene.

7. Action of quinoline on (IV). 8 g of the bromide prepared in section 3 above and 12 g quinoline were cautiously heated in a Wurtz flask until the reaction started; it then proceeded intensively without heating. The distillate, coming over at 78-120°, was washed with dilute sulfuric acid and water and dried with calcium chloride. After two distillations over metallic sodium (to bind the bromides) a transparent liquid was obtained which crystallized at −5 to −7° and did not contain halogen. Weight 1.8 g or 69.1%.

B.p. 78-82°; bromine number 4.0; d_4^{16} 0.8800; n_D^{16} 1.5017. The spectroscopic examination indicated a content of 90-95% benzene.

SUMMARY

1. Interaction of 1,3-cyclohexadiene with quinoline dibromide gives dibromocyclohexene. It is shown that quinoline acts on the bromide formed to give benzene.

2. Heating of quinoline hydrobromide dibromide with 1,3-cyclohexadiene gives tetrabromocyclohexane. Among the products of interaction of the tetrabromide with quinoline is bromobenzene.

3. The main product of reaction of 1,3-cyclohexadiene with quinoline hydrobromide dibromide in the cold is dibromocyclohexene.

4. Reaction of 1,3-cyclohexadiene with quinoline tetrabromide in the cold leads to a mixture of approximately equal parts of dibromocyclohexene and tetrabromocyclohexane.

5. The experimental data are in full accord with the scheme previously put forward by one of us [3] and may serve as confirmation of the last two stages of the scheme.

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THE ACTION OF AMMONIA ON 1-HYDROXYANTHRAQUINONE

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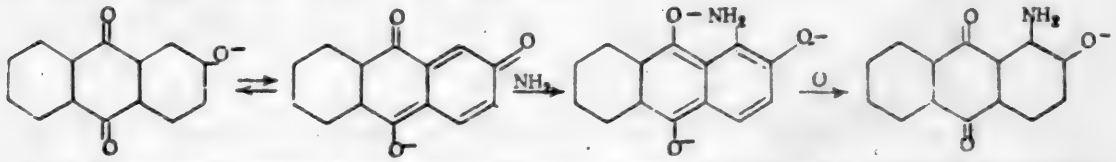
Derivatives of anthraquinone containing amino groups in the α-position, especially 1-amino- and 1,5-diaminoanthraquinones, are most important starting materials for the synthesis of other dyes (vat and acid dyes for acetate and synthetic fiber and pigment dyes). The only technical method for the preparation of these derivatives is the ammonolysis of the corresponding anthraquinone sulfonic acids. However, not even the most successful industrial methods of preparation secures complete transformation of the sulfonic acid into amino compound [1]. A yield of 100% 1-aminoanthraquinone represents 62% of the theoretical; a yield of 100% 1,5-diaminoanthraquinone represents 62% of the theoretical.

Due to the high concentration of hydroxyl ions in aqueous ammonia, formation of hydroxy derivatives of anthraquinone is always observed, as well as substitution of the sulfo group by the amino group.

Attention to the absence of a fully satisfactory method of preparation of 1-aminoanthraquinone was drawn by Fierz-David [2] in his well-known book.

A patent was recently announced for the preparation of α-amino derivatives of anthraquinone by heating the corresponding sulfonates with ammonium salts of arsenic acid at pH values in the vicinity of 7, which enables the preparation of amino derivatives of high quality; the yield of 1-aminoanthraquinone reaches 98.7% (at pH 7.3) and that of 1,5-diaminoanthraquinone 85% (at pH 7) [3]. This method is inconvenient, however, on the industrial scale, because of the employment of a large amount of arsenic compounds.

In a study of the ammonolysis of 2-chloroanthraquinone by aqueous ammonia [4], one of us found that the principal by-product of the reaction, which is soluble in aqueous ammonia, is 1-amino-2-hydroxyanthraquinone. It transpired that on interaction of 2-hydroxyanthraquinone with ammonia in milder conditions than those necessary for transformation of 2-chloroanthraquinone into 2-aminoanthraquinone, substitution of hydrogen takes place in the 1-position of the anthraquinone nucleus. Simultaneously, the carbonyl groups are reduced as in the well-known addition of ammonia and amines to benzoquinone.



It was of interest to investigate the possibility of a similar reaction in the case of α-substituted anthraquinone.

Heating of 1-hydroxyanthraquinone with ammonia gave a product soluble in alkalies and containing nitrogen. Chromatographic separation of the chlorobenzene solution of this product on alumina as the sole component yielded a substance with m.p. 257-258° and with an elementary analysis corresponding to an aminohydroxyanthraquinone.

Regarding here, as in the case of 2-hydroxyanthraquinone, the process of substitution of hydrogen by the amino group as the addition of ammonia to the tautomeric form of the hydroxyanthraquinone ion, we can expect the amino group to enter the anthraquinone nucleus in the 2-, 3-, or 4-position. We know that in the action of aniline on o-benzoquinone, the phenylamino group enters in the para-position to the carbonyl groups [5]. In the action of metal arylides on α-amino derivatives of anthraquinone, substitution of hydrogen occurs in the 4-position [6]. Alkaline fusion of 1-hydroxyanthraquinone, which must be regarded as an analogous process, leads to formation of alizarin [7].

The substance obtained by the action of aqueous ammonia on 1-hydroxyanthraquinone had properties similar to those of 1-hydroxy-2-aminoanthraquinone. The latter was synthesized by Perger, Scholl and others by reacting

aqueous ammonia with alizarin [8]; Benda prepared it from 3-nitro-4-hydroxy-1-anthraquinonyl-amonic acid (m.p. about 250°) [9]; Kopetschni prepared it from 2-acetamino-1-acetoxyanthraquinone (m.p. 257-258°) [10]; Brass and Ziegler prepared it by decomposition of 2-anthraquinonyl-alizarin in concentrated sulfuric acid (m.p. 226-227°) [11].

With the aim of identifying the prepared compound, the synthesis was effected of 1-hydroxy-2-aminoanthraquinone by amination of alizarin followed by purification of the product by chromatography on alumina. The purified substance melted at 257-258° and proved to be identical with the compound prepared from 1-hydroxyanthraquinone.

Consequently, the main direction of the reaction of 1-hydroxyanthraquinone with aqueous ammonia may be represented by a scheme of the above type.

1-Hydroxy-2-aminoanthraquinone was detected among the products of ammonolysis of 1-anthraquinonesulfonic acid. The products soluble in aqueous ammonia were isolated by acidification and were chromatographed on alumina in chlorobenzene solution. Chromatographic examination of technical 1-aminoanthraquinone likewise revealed the presence of 1-hydroxy-2-aminoanthraquinone.

EXPERIMENTAL

1-Hydroxyanthraquinone was prepared by diazotization of 1-aminoanthraquinone and decomposition of the diazo compound by Ullmann's method [12]; m.p. 191-192°.

1-Hydroxy-2-aminoanthraquinone from 1-hydroxyanthraquinone. 20 g 1-hydroxyanthraquinone is heated for 6 hours at 131-140° with 273 g 25% aqueous ammonia. To the reaction mass is added 50 ml 2% sodium hydroxide solution, thoroughly stirred and filtered. An insoluble black precipitate is collected on the filter. The violet solution is acidified with hydrochloric acid and a reddish-brown flocculent precipitate is formed. Weight of dry precipitate 1.35 g, m.p. 218-223°. Treatment of the insoluble precipitate with 1500 ml 2% sodium hydroxide at 60° followed by acidification of the solution gives an additional 0.35 g reddish-brown product with m.p. 207-224°. The precipitates are combined. A solution of 1.2 g of the mixture in 1900 ml chlorobenzene is subjected to chromatographic separation on alumina. Several colored bands are formed. The main broad band (blue-violet) is separated and the adsorbed substance is eluted with 4% sodium hydroxide solution. Acidification of the reddish-violet alkaline solution gives 0.5 g brown-red material with m.p. 257-258° (from glacial acetic acid). The compound dissolves in alcohol with a yellowish-red color, in ether with an orange color, in NaOH solution with red-violet color and in concentrated sulfuric acid with a brown color (according to Brass and Ziegler the solution in concentrated sulfuric acid is olive green). It readily forms a hydrosulfite-alkali vat with an orange color. With baryta water it gives an insoluble blue-violet precipitate.

Found %: C 69.51, 70.71; H 3.92, 3.94; N 6.18, 6.25. $C_{14}H_9O_3N$. Calculated %: C 70.27; H 3.79; N 5.86

1-Hydroxy-2-aminoanthraquinone from alizarin. 8 g alizarin is heated with 135 g 30% aqueous ammonia for 5 hours at 150°. The reaction mass is filtered, and acidified with hydrochloric acid to give a reddish-brown precipitate with a dry weight of 1.55 g and m.p. 218-234°.

Chromatographic separation of the chlorobenzene solution yielded 0.47 g of brownish-red substance with m.p. 257-258° (from glacial acetic acid). No depression occurred in a mixed melting test with the substance prepared from 1-hydroxyanthraquinone.

Found %: C 69.94, 69.73; H 4.02, 3.93; N 5.91, 6.05. $C_{14}H_9O_3N$. Calculated %: C 70.27; H 3.79; N 5.86.

SUMMARY

1. The action of aqueous ammonia on 1-hydroxyanthraquinone gives 1-hydroxy-2-aminoanthraquinone.

2. 1-Hydroxy-2-aminoanthraquinone is formed as a by-product in the ammonolysis of 1-anthraquinonesulfonic acid.

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ACYLATION WITH THE AID OF VINYL ACETATE

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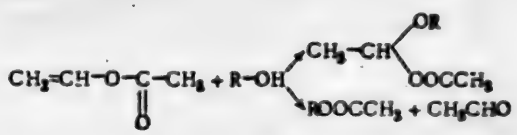
We have previously described the interaction of vinyl acetate with amines [1] which showed vinyl acetate to be a convenient acetylating agent with selective action.

M. F. Shostakovsky showed [2] that in presence of mercuric salts alcohols add on to vinyl acetate at the double carbon-carbon bond with formation of acetates of polyacetals (so-called acylals), whereas in the case of tertiary alcohols, acetates are obtained.

Consequently, depending upon the structure of the original alcohol, the reaction may proceed in two directions



It is reported in the patent literature that secondary alcohols [3] and phenols, in presence of alkaline agents, are acetylated by vinyl acetate.

We carried out several experiments on the interaction of vinyl acetate with alcoholates and found that by this means it was possible to acetylate not only secondary but also primary alcohols. The reaction proceeds very energetically and is accompanied by polymerization, as well as by secondary formation of sodium acetate (even when the reaction is performed with cooling or in solvents), so that excess of vinyl acetate is needed for satisfactory yields.

Regarding the character of the polymer formed, it is evidently an alcoholate of polyvinyl alcohol since it dissolves easily in water and alcohol.

It proved to be most advantageous to use as the solvent an excess of the alcohol to be acetylated, which itself does not react with vinyl acetate. All the experiments were run in comparable conditions, i.e., to the prepared alcoholate (0.05 g-atom sodium was dissolved in 0.1 mole alcohol) was carefully added 0.1 mole vinyl acetate at 0°.

It was found that furfuryl alcohol, which possesses an allenic structure, gives a nearly quantitative yield of acetate (reckoned on the alcoholate brought into reaction), but in the same conditions allyl alcohol gives only a considerable amount of resin, possibly due to copolymerization both of the alcohol itself and of its acetate with the vinyl compounds. Still more interesting is the fact that cyclohexanol gave a good yield of acetate – 40.5% of the theoretical (81% reckoned on the alcoholate) – whereas 3-hexanol, which contains the same number of carbon atoms and is also a secondary alcohol, is totally recovered from the reaction unchanged. In the case of β-phenylethyl alcohol, the acetate is obtained in a yield of 18% of the theoretical (36% reckoned on the alcoholate).

By analogy with isopropenyl acetate [5] we attempted to perform the acetylation of alcohols with the help of acidic agents. By heating in presence of sulfuric acid, vinyl acetate was also found to acetylate alcohols. In these conditions phenol gives a product of the polycondensation type (phenol-aldehyde resins). Acetylation of isopropyl alcohol (yield 39%) and of dimethylethylcarbinol (yield 43%) is accompanied by formation of a considerable amount of olefin (due to dehydration).

In all the experiments, the catalyst was used in the proportion of 3-5% by weight of the alcohol; the alcohol and vinyl acetate were in equivalent amounts. The mixture of components was heated 6-8 hours to 100-110°.

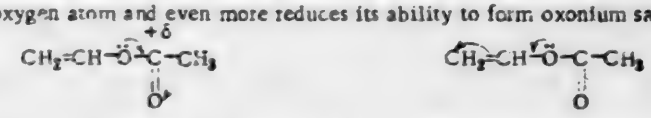
In these conditions allyl alcohol is appreciably resinified and enters incompletely into the reaction; the yield is 22% of the theoretical (40% reckoned on the alcohol used); cyclohexanol gives 35% (65%) yield; 1-ethoxy-2-propanol 35% (68%); 1-hexanol 49% (80%).

With 1-hexanol several experiments were carried out with the objective of establishing the effect of both the conditions and the catalysts on the yield of acetate. It was found that the introduction of double the amount of vinyl acetate raised the yield to 69%. Other catalysts were also tried out. In presence of aluminium sulfate the yield was 64% (for equivalent amounts of alcohol and vinyl acetate). Aluminum ethylate was also tried since we thought that the acetaldehyde would partially disproportionate by a Tishchenko reaction [6] and thereby appreciably raise the yield of acetate. Aluminum ethylate proved, however, to be too weak a catalyst. The yields did not exceed 12%. Ethyl acetate was not detected among the products of the reaction in experiments in an open vessel or in sealed ampoules.

Consequently, vinyl acetate can serve as a convenient acetylating agent for amines and alcohols. Due, however, to its selectivity, it has some advantages over ketenes, although the yields of acetates in our case are considerably lower. We, therefore, decided to test the acetylating action of vinyl esters of other acids in cases where the preparation of the corresponding ketene is either impossible or involves great difficulties. From vinyl acetate we therefore prepared vinyl butyrate and vinyl benzoate by treatment with the respective alcohols in presence of mercuric salts [5, 7]. It was found that vinyl butyrate, in analogy with vinyl acetate, readily forms butyraldehyde together with little resin (with equivalent amounts the yield is 70%). In the absence of catalyst, vinyl benzoate does not react with aniline at room temperature; the addition of a little sulfuric acid, however, provokes a vigorous reaction and the yield of benzanilide, with equimolar quantities, reaches 82%. Consequently, not only vinyl acetate, but also vinyl esters of other carboxylic acids can be utilized as acylating agents.

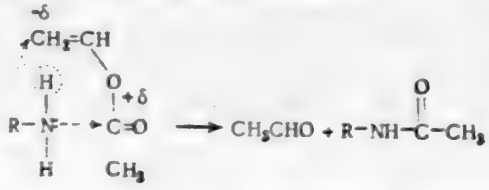
In order to explain the mechanism of acetylation with vinyl acetate, we must take into consideration the reciprocal influence of the atoms in the vinyl acetate molecule. It is obvious that the oxygen atom located between the vinyl and the carbonyl group is weakened in its complex-forming properties due to the influence of the carbonyl group, and nucleophilic agents will be the most likely to attack the carbonyl carbon atom. This is actually observed in the action of amines or alcoholates.

The matter is rather more complicated when we consider the vinyl portion of the molecule, which likewise influences the ethereal oxygen atom and even more reduces its ability to form oxonium salts.



It follows from the above schemes that the CH_2 group in the vinyl acetate molecule is rather more electronegative than the CH group and, consequently, electrophilic agents are bound to preferentially attack the methylene group, although the carbonyl group also weakens the above-indicated polarization of the bond.

In practice, the action of strong acids on vinyl acetate (proton attack) leads to cleavage of acetaldehyde. The mercury group also acts on the methylene and not on the methine group [8]. Finally, sulfonation of vinyl butyl ether and of vinyl acetate by pyridine- and dioxanesulfotrioxide [9] leads to sulfoacetaldehyde, which fact also is consistent with the presence of a certain negative charge at the methylene group. Consequently, if nucleophilic agents (such as amines) attack vinyl acetate, then acetylation takes place. At first, the nucleophilic agent attacks the carbonyl carbon atom, while subsequently we get stabilization of the intermediate complex due to migration of a proton and cleavage of a molecule of acetaldehyde.



The ease of acetylation is governed primarily not by the mobility of the hydrogen atom but by the nucleophilism of the agent.

In the interaction of vinyl acetate with alcohols, the direction of the process depends on the conditions and on the structure of the alcohol. The nucleophilic properties of alcohols are markedly weakened by the phenomenon of association (hydrogen bond). If this bond is broken (say by conversion of the alcohols into alcoholates), then acetylation will take place. This can be demonstrated by adding acidic agents which facilitate cleavage of acetaldehyde.

If, however, the reaction of vinyl acetate with alcohols proceeds in presence of mercury salts, the primary process is mercuration a the double carbon-carbon bond which leads ultimately not to acetates but to acylals. In

the case, however, of tertiary alcohols, which are more strongly nucleophilic than primary alcohols, the principal process, even in presence of mercury salts, is acylation.

EXPERIMENTAL

Acetylation of isopropyl alcohol. Into a two-necked flask fitted with stirrer and reflux condenser was introduced 6.0 g (0.1 mole) isopropyl alcohol, 8.6 g (0.1 mole) vinyl acetate and 4 drops sulfuric acid. The mixture was heated for 8 hours with stirring on an oil bath at 100-110°. Propene, identified as dibromide, was detected in the escaping gases. After this period, the mixture was dried with potassium carbonate and distilled in a low column to give 4.0 g isopropyl acetate or 39% of the theoretical. B.p. 87.5-88° at 753 mm.

n_D^{20} 1.3715; d_4^{20} 0.8740; MR_D 26.77; calculated 26.94.

Acetylation of dimethylethylcarbinol. By the same procedure, starting from 8.8 g (0.1 mole) dimethylethylcarbinol and 8.6 g vinyl acetate in presence of sulfuric acid, 5.5 g acetate was obtained. Yield 42% of theoretical. B.p. 121-124° at 740 mm. A second distillation gave b.p. 124-125° at 749 mm.

n_D^{20} 1.4010; d_4^{20} 0.8740; MR_D 36.16; calculated 36.18.

Acetylation of allyl alcohol. From 11.6 g (0.2 mole) allyl alcohol and 17.2 g (0.2 mole) vinyl acetate in presence of 5-6 drops sulfuric acid was obtained 4.4 g allyl acetate (22% of the theoretical yield). B.p. 102-103° at 762 mm.

n_D^{20} 1.4043, d_4^{20} 0.9272; MR_D 26.41; calculated 26.47.

Literature data: b.p. 103-104°; n_D^{20} 1.40488; d_4^{20} 0.9276 [10].

On adding vinyl acetate (16.2 g) to sodium allylate (2.3 g sodium in 11.6 g allyl alcohol) at 0°, very serious resinification is observed and no allyl acetate could be isolated from the products of reaction.

Acetylation of 1-hexanol. A) The reaction was conducted as in the preceding experiments (in presence of sulfuric acid). From 10.3 g (0.1 mole) 1-hexanol and 8.6 g vinyl acetate (0.1 mole) was obtained, after fractionation, 4.1 g of the original alcohol and 7.0 g acetate. Yield 49% of the theoretical (80% reckoned on the alcohol consumed). On introducing into the reaction an excess of vinyl acetate (17.2 g) the yield rises to 69%. B.p. 169-170° at 767 mm.

n_D^{20} 1.4115; d_4^{20} 0.8770; MR_D 40.83; calculated 40.88.

Literature data: b.p. 169.2°; d_0^0 0.8902 [11].

B) A mixture of 10.3 g 1-hexanol and 8.6 g vinyl acetate was heated with 0.3 g anhydrous aluminium sulfate in a sealed ampoule for 20 hours at 100-105°. Fractional distillation gave 3 g acetaldehyde (b.p. 21-24°, silver mirror test) and 9.2 g acetate. Yield 64% of the theoretical. B.p. 167-168° at 749 mm; n_D^{20} 1.4110.

C) A mixture of 10.3 g 1-hexanol, 8.6 g vinyl acetate and 0.5 g aluminum ethylate was heated in a sealed ampoule for 20 hours at 100-105°. Fractional distillation gave 1.7 g acetate. Yield 12% of theoretical. B.p. 168-169° at 758 mm.

Acetylation of 3-hexanol. From 9.0 g (0.09 mole) 3-hexanol and 7.7 g (0.09 mole) vinyl acetate in presence of 5-6 drops sulfuric acid after 8 hours' heating on an oil bath was obtained 3.6 g original alcohol and 6.5 g acetate. Yield 47% of the theoretical (85% reckoned on the alcohol consumed). B.p. 149-150° at 758 mm.

n_D^{20} 1.4061; d_4^{20} 0.8670; MR_D 40.83; calculated 40.80.

Literature data: b.p. 149-151°; n_D^{20} 1.4037; d_4^{20} 0.8672 [12].

On adding vinyl acetate to a solution of the sodium compound of 3-hexanol, considerable heat was developed; after extraction, however, of the reaction mixture with absolute ether followed by distillation of the extract, the original 3-hexanol was recovered and none of its acetate was detected.

Acetylation of cyclohexanol. A) 20.0 g (0.2 mole) cyclohexanol is placed in a three-necked flask fitted with stirrer and reflux condenser: addition is made with stirring of 2.3 g (0.1 g-atom) sodium in small pieces. After the metal has dissolved (1 hour at 110°) dropwise addition is made with cooling to the mixture (cooled to 0°) of 17.2 g (0.2 mole) vinyl acetate. After dilution with ether and separation of the precipitate, the liquid is distilled to give 11.5 g acetate. Yield 40.5% of the theoretical (81% reckoned on the alcoholate). B.p. 96-97° at 85 mm.

n_D^{20} 1.4432; d_4^{20} 0.9664; MR_D 38.92; calculated 38.59.

B) A mixture of 10.0 g (0.1 mole) cyclohexanol, 8.6 g vinyl acetate (0.1 mole) and 5-8 drops concentrated sulfuric acid was heated with stirring on an oil bath at 100-110° for 8 hours. Distillation gave 5.0 g cyclohexyl acetate. Yield 35% of theoretical (65% reckoned on the alcohol consumed). B.p. 98-100° at 82 mm; n_D^{20} 1.4435; d_4^{20} 0.9665.

Acetylation of 1-ethoxy-2-propanol. From 10.4 g (0.01 mole) 1-ethoxy-2-propanol and 8.6 g (0.1 mole) vinyl acetate in presence of 5 drops sulfuric acid was obtained 5.1 g of the original alcohol and 3.2 g acetate. Yield 35% of theoretical (68% reckoned on the alcohol consumed). B.p. 164-165° at 758 mm.

n_D^{20} 1.4081; d_4^{20} 0.09456; MR_D 38.42; calculated 38.82.

Literature data: b.p. 158-160°; n_D^{20} 1.4097; d_4^{20} 0.9462 [13].

Acetylation of β-phenylethyl alcohol. In 12.2 g (0.1 mole) β-phenylethyl alcohol was dissolved 1.1 g (0.05 mole) metallic sodium. To the cooled (to 0°) mixture, dropwise addition was then made, with stirring and cooling of 8.6 g (0.1 mole) vinyl acetate. Sodium acetate was precipitated by adding ether and filtered off. Distillation of the filtrate gave 3.0 g acetate. Yield 18% of the theoretical (30% reckoned on the alcoholate). B.p. 110-111° at 18 mm.

n_D^{20} 1.5115; d_4^{20} 1.044; MR_D 47.14; calculated 46.43.

Literature data: b.p. 224°; 118-129° at 13 mm; n_D^{20} 1.5108 [14].

Acetylation of furfuryl alcohol. By the same procedure, using 9.8 g (0.1 mole) furfuryl alcohol, 8.6 g (0.1 mole) vinyl acetate and 1.1 g (0.05 g-atom) sodium, 7.0 g furfuryl acetate was obtained. Yield about 50% of theoretical (98% reckoned on the alcoholate). B.p. 83-85° at 15 mm.

n_D^{20} 1.4662; d_4^{20} 1.1117; MR_D 34.89; calculated 34.69.

Literature data: b.p. 175-177°; d_4^{20} 1.1176 [15].

Preparation of vinyl benzoate. A mixture of 34.4 g (0.4 mole) vinyl acetate, 24.4 g (0.2 mole) benzoic acid, 0.4 g mercuric acetate and 2 drops sulfuric acid was heated with stirring for 24 hours at 45-50°. A suspension of 20 g sodium carbonate in 50 ml water was then added and the organic layer was separated. The ether was distilled off and the residue distilled in vacuum to give 11.9 g (41%) vinyl benzoate. B.p. 98-100° at 24 mm.

n_D^{20} 1.5282; d_4^{20} 1.0685; MR_D 42.65; calculated 41.34.

Literature data: b.p. 72-73° at 3 mm; n_D^{20} 1.5279; d_4^{20} 1.069 [8].

Preparation of vinyl butyrate. From 8.8 g butyric acid, 17.2 g vinyl acetate, 0.22 g mercuric acetate and 1 drop sulfuric acid, using the same procedure, was obtained 5.8 g (51%) vinyl butyrate. B.p. 115-116° at 774 mm.

n_D^{20} 1.4096; d_4^{20} 0.8966; MR_D 31.25; calculated 31.19.

Found %: C 63.14, 63.19; H 8.80, 8.87. $C_6H_{10}O_2$. Calculated %: C 63.21; H 8.84.

Reaction of aniline with vinyl benzoate. To a mixture of 2.3 g (0.025 mole) aniline and 3.7 g (0.025 mole) vinyl benzoate was added 2 drops concentrated sulfuric acid. After the spontaneous heating had ceased, the mixture was heated for 30 minutes to 100-120°; the cooled mixture crystallized. The reaction product was pulverized, washed with hydrochloric acid and recrystallized from alcohol. Yield 3.5 g (71%) benzanilide. M.p. 160-161° in agreement with the literature.

Similarly (but without addition of sulfuric acid), 2.8 g aniline and 3.7 g vinyl butyrate gave 4.0 g (82%) butyranilide. M.p. 92° in agreement with the literature.

SUMMARY

1. The acylation is described of alcohols with the help of vinyl acetate which proceeds both in an acidic and an alkaline medium. A mechanism for the reaction is proposed.

2. The employment of vinyl esters of other acids as acylating agents is demonstrated with reference to the acylation of aniline with vinyl benzoate and vinyl butyrate.

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• See Consultants Bureau Translations, page 779.

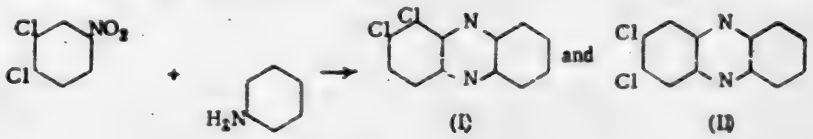
SYNTHESIS OF HALOGEN DERIVATIVES OF PHENAZINE

II. DICHLOROPHENAZINES

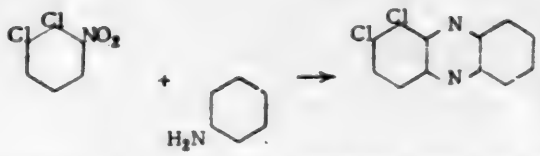
V. P. Chernetsky and A. I. Kiprianov

In the previous communication [1], the synthesis was described of mono- and dichlorophenazines by alkaline condensation of chloronitrobenzenes with aniline and chloroanilines *. In the present paper we describe the synthesis and properties of five new bases: 1,2-, 1,3-, 1,4-, 2-3- and 2,7-dichlorophenazines, and some of their N-oxides. We thus now know all ten of the possible isomers of dichlorophenazine. In this paper are also described the 4 isomeric dichloronitrodiphenylamines, which we prepared at the same time as the above-enumerated phenazines.

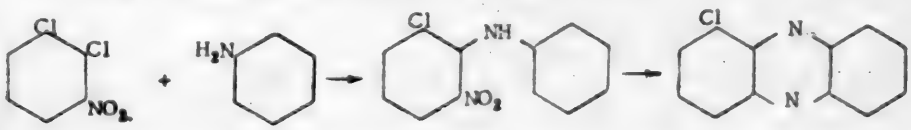
The synthesis and proof of structure of the new dichlorophenazines were carried out by the following methods. 1,2-Dichlorophenzine was prepared by condensation of 3,4-dichloronitrobenzene [3] with aniline in presence of powdered KOH. As we see from the reaction scheme



the formation is possible of a mixture of two isomers (I) and(II). Chromatographic treatment of the reaction product yielded only one light-yellow base with m.p. 175-177° and one bright-yellow N-oxide which melted with decomposition at 217-219°. Reduction of the N-oxide with tin chloride in hydrochloric acid gave the same dichlorophenazine with m.p. 175-177°. In order to solve the problem of the structure of this base, we performed the alkaline condensation of 2,3-dichloronitrobenzene with aniline, which we assumed must lead only to 1,2-dichlorophenazine



The resultant phenazine derivative, however, melted at 120-122° and did not give a depression with 1-chlorophenazine. Evidently the mobile chlorine atom in the 2-position had split off in the first stage of the condensation

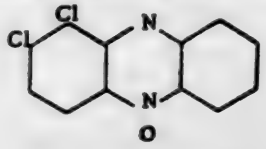


Dichlorophenazine could not be detected among the products of this experiment.

We then investigated the condensation of 3,4-dichloroaniline with nitrobenzene. Here the possibility of loss of a chlorine atom was excluded and the formation was to be expected of the very same isomeric dichlorophenazines (I and (II) as in the first condensation. Actually in this case, again, only one dichlorophenazine was obtained, but it differed from the first in having a much higher (250-251°) melting point. The different melting points alone suffice to indicate that the isomer with the higher melting point has the more symmetrical structure (II) and the one with the lower melting point the less symmetrical structure (I). The structure of the base with m.p. 250-251° was conclusively established by its transformation into the dihydroxy derivative and then into the diacetoxy derivative with m.p. 239-240°. A diacetoxy derivative with the same melting point was obtained from 2,3-dihydroxy-

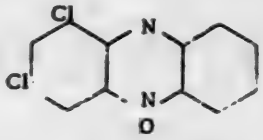
* After the present paper had gone to press, a paper appeared which described the synthesis of 1,5-dichlorophenazine by the same method [2].

phenazine which in turn was prepared from 2,3-diaminophenazine by the method of Fischer and Hepp [4]. A mixed test with both diacetyl derivatives did not give a depression. It was thus proved that the base with m.p. 250-251° is 2,3-dichlorophenazine; consequently, its isomer with m.p. 175-177° is 1,2-dichlorophenazine; the N-oxide with m.p. 217-219° (with decomposition), obtained in the first condensation, was evidently the oxide of 1,2-dichlorophenazine. We did not establish the actual position of the oxygen atom in this and the subsequently described N-oxides. In a paper by Pushkareva and Agibalova [5], and later in one by Pachter and Kloetzel [2], it was shown that the NO group in N-oxides of phenazines is formed on alkaline condensation of amines with nitro compounds at the expense of the nitro group. Consequently, in our case, the 10-(N)-oxide of 1,2-dichlorophenazine (a) was obtained. 1,3-Dichlorophenazine was isolated by condensation of 3,5-dichloronitrobenzene [6] with aniline.



(a)

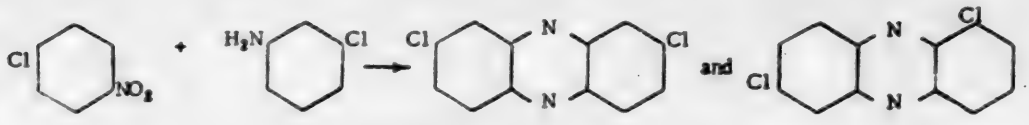
Chromatographic separation of the condensation products on alumina gave, apart from the base, its N-oxide, to which in accordance with the above considerations, we must ascribe the structure of the 10-(N)-oxide of 1,3-dichlorophenazine (b)



(b)

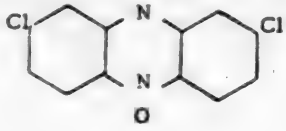
1,4-Dichlorophenazine was synthesized by condensation of 2,5-dichloronitrobenzene with aniline.

Alkaline condensation of p-nitrochlorobenzene with m-chloroaniline could yield two isomeric dichlorophenazines: 1,6- and 2,7-dichlorophenazines (IV) and (III)



(III) (IV)

1,6-Dichlorophenazine (IV) with m.p. 171-173° was prepared by us previously [1]. The above condensation scheme yielded only one dichlorophenazine with m.p. 229-230° which was consequently 2,7-dichlorophenazine (III). A yellow N-oxide was also isolated which melted with decomposition at 232-233° and on reduction with tin chloride was transformed into the same 2,7-dichlorophenazine. In the light of the previous considerations, this N-oxide must be the 10-(N)-oxide of 2,7-dichlorophenazine (c)



(c)

In Table 1 are listed the mono- and dichlorophenazines which we prepared by alkaline condensation, together with the starting materials and yields.

The yields set forth in Table 1 are not optimum. There is no doubt that the yields could be raised by suitable choice of conditions of condensation for each individual derivative. It is noteworthy that N-oxides are only formed in those cases where a chlorine atom is not adjacent to the NO group.

TABLE 1

Starting compounds: Nitro compound	Starting compounds: Amine	Chlorophenazines obtained	Yield in % of theory: Of individual compounds	Yield in % of theory: Total
o-Nitrochlorobenzene	Aniline	1-Chlorophenazine	12.4	
	o-Chloroaniline	1,5-Dichlorophenazine	8.1	
	m-Chloroaniline	1,6-Dichlorophenazine	10.4	26.8
		1,8-Dichlorophenazine	16.4	
	p-Chloroaniline	1,7-Dichlorophenazine	10.5	
p-Nitrochlorobenzene	Aniline	10-(N)-oxide of 2-chlorophenazine	16	
	m-Chloroaniline	2,7-Dichlorophenazine	11.4	13.9
		10-(N)-oxide of 2,7-dichlorophenazine	2.5	
	p-Chloroaniline	10-(N)-oxide of 2,6-dichlorophenazine	17	
Nitrobenzene	3,4-Dichloroaniline	2,3-Dichlorophenazine	2	
2,3-Dichloronitrobenzene	Aniline	1-Chlorophenazine	8	
2,5-Dichloronitrobenzene	Aniline	1,4-Dichlorophenazine	24	
3,4-Dichloronitrobenzene	Aniline	1,2-Dichlorophenazine	6.8	
		10-(N)-oxide of 1,2-dichlorophenazine	10.2	17
3,5-Dichloronitrobenzene	Aniline	1,3-Dichlorophenazine	10.0	
		10-(N)-oxide of 1,3-dichlorophenazine	11.0	21

In Table 2 are listed the 12 possible mono- and dinitrophenazines and their melting points.

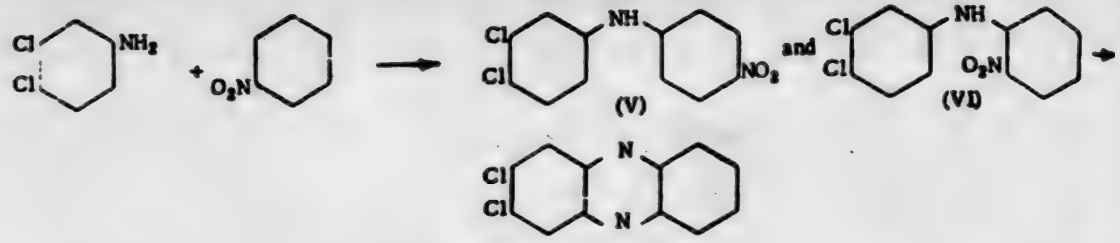
TABLE 2

Chlorophenazines	M.p.	Literature
1-Chlorophenazine	122-123	Wrede and Mulroth [7]
2-Chlorophenazine	140-141	McCombie et. al., [8]
1,2-Dichlorophenazine	175-177	
1,3-Dichlorophenazine	191-192	V. P. Chernetsky and A. L. Kiprianov*
1,4-Dichlorophenazine	198-199	
1,5-Dichlorophenazine	271-272	V. P. Chernetsky, S. B. Serebryany [1]; Pachter and Kloetzel [2]
1,6-Dichlorophenazine	171-173	
1,7-Dichlorophenazine	222-223	V. P. Chernetsky [1]
1,8-Dichlorophenazine	211-212	
2,3-Dichlorophenazine	250-251	V. P. Chernetsky and A. L. Kiprianov*
2,6-Dichlorophenazine	266-267	Bamberger, Ham [9]
2,7-Dichlorophenazine	227-228	V. P. Chernetsky and A. L. Kiprianov*

Omitted from Table 2 is the dichlorophenazine with m.p. 144° described by Claus in 1875 [10]. Claus had evidently obtained a mixture of isomers which he failed to resolve.

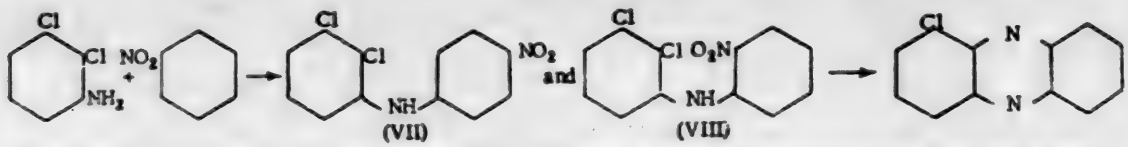
As indicated at the start of the present communication, several dichloronitrodiphenylamines were isolated from the products of alkaline condensation. Condensation of 3,4-dichloroaniline with nitrobenzene gave, apart from 2,3-dichlorophenazine, two isomeric dichloronitrodiphenylamines – reddish-orange with m.p. 161-162° and yellow with m.p. 214-215°. Formation of derivatives of diphenylamine in the alkaline condensation of nitro compounds with amines must clearly be regarded as the first stage in the synthesis of phenazines

*See this paper



The more deeply colored product with m.p. 161-162° proved to be identical with 3,4-dichloro-2'-nitrodiphenylamine (VI), which we prepared by heating 3,4-dichloroaniline with o-nitrochlobenzene in presence of sodium acetate [11]. Consequently, we must ascribe the structure of 2,3-dichloro-4'-nitrodiphenylamine (V) to the yellow preparation with m.p. 214-215°.

Condensation of 2,3-dichloroaniline with nitrobenzene was also performed. This condensation proceeded with displacement of an atom of chlorine and gave 1-chlorophenazine. From the reaction products were isolated two isomeric dichloronitrodiphenylamines, one of which was orange-red with m.p. 147-148°, and the other yellow with m.p. 156-157°. In accordance with the reaction scheme



a... taking into account the fact that o-nitroamines are more deeply colored than p-nitroamines, we should ascribe to the preparation with m.p. 147-148° the constitution of 2,3-dichloro-2'-nitrodiphenylamine (VIII), and to the preparation with m.p. 156-157° the constitution of 2,3-dichloro-4'-nitrodiphenylamine (VII).

Small quantities of diphenylamine derivatives were formed in all our condensations. The yield of these secondary or intermediate products can be raised by introducing a 2- or 3-fold excess of nitro component into the alkaline condensation with the amine.

EXPERIMENTAL

The procedure used in this investigation for the condensation of aromatic nitro compounds with amines was the same as in the preceding communication with the sole difference that it was found possible to limit the duration of condensation to 3 hours without detriment to the yield. For purification of the reaction products, steam distillation from the alkaline mixture of the toluene and unreacted nitro and amino components was excluded because it was observed that the amount of resin increased on distillation in presence of alkali. At the conclusion of the heating, the toluene solution was filtered off and the alkaline residue extracted with small portions of boiling toluene. The solvent was driven off from the combined toluene solutions and the residue chromatographed on alumina. For the purpose of complete separation the chromatographic treatment from benzene, chloroform or dichloroethane solutions was repeated 2-3 times. The substances isolated by the chromatographic separation were recrystallized.

1-Chlorophenazine was prepared by condensation of 1.8 g 2,3-dichloronitrobenzene with 0.88 g aniline in presence of 3.7 g powdered KOH in 15 ml toluene. Yield 0.112 g (6% of the theoretical); pale-yellow needles from alcohol, m.p 121-122°.

1,2-Dichlorophenazine was synthesized from 11.2 g 3,4-dichloronitrobenzene and 9.3 g aniline in 150 ml toluene in presence of 28.5 g powdered KOH. Chromatographic treatment of the chloroform solution and recrystallization from dichloroethane gave 1.68 g (6.8%) 1,2-dichlorophenazine in the form of clusters of light-yellow small needles, m.p. 175-177°.

Found %: N 11.08, 11.14; Cl 28.80, 28.77. $C_{12}H_6N_2Cl_2$. Calculated %: N 11.24; Cl 28.51.

10-(N)-oxide of 1,2-dichlorophenazine was obtained in the same experiment by chromatographing of the products. Long, bright-yellow needles from dichloroethane. Yield 2.7 g (10.2%), m.p. 217-219° (with decomposition).

Found %: N 10.59, 10.60; Cl 26.50. $C_{12}H_6ON_2Cl_2$. Calculated %: N 10.57; Cl 26.79.

2,3-Dichlorophenazine was prepared by heating a mixture of 32.4 g 3,4-dichloroaniline, 73.8 g nitrobenzene, 100 g powdered KOH and 300 ml toluene. Crystallization from dichloroethane gave 0.95 g (2%) light-yellow needles, m.p. 250-251°.

Found %: N 11.29, 11.37; Cl 28.57. $C_{12}H_6N_2Cl_2$. Calculated %: N 11.24; Cl 28.51.

1,3-Dichlorophenazine was prepared by heating a mixture of 19.2 g 3,5-dichloronitrobenzene, 9.3 g aniline, 28.5 g powdered KOH and 150 ml toluene. After chromatographing and crystallization from alcohol, there was obtained 2.5 g (10%) pale-yellow, small needles, m.p. 191-192°.

Found %: N 11.11, 11.02; Cl 28.22. $C_{12}H_6N_2Cl_2$. Calculated %: N 11.24; Cl 28.51

1-(N)-oxide of 1,3-dichlorophenazine was obtained in the same experiment by chromatogramming of the products from dichloroethane. Crystallization gave 2.8 g (11%) bright-yellow, slender, small needles, m.p. 236-237° (with decomposition).

Found %: N 10.59, 10,71; Cl 26.43, 26.67. $C_{12}H_6ON_2Cl_2$. Calculated %: N 10.57; Cl 26.79.

1,4-Dichlorophenazine was prepared from 19.2 g 2,5-dichloronitrobenzene, 9.3 g aniline, 28.5 g powdered KOH and 150 ml toluene. Yield 6 g (24%). Long yellow needles (from dichloroethane), m.p. 198-199°.

Found %: N 11.02, 11.20; Cl 28.48, 28.85. $C_{12}H_6N_2Cl_2$. Calculated %: N 11.24; Cl 28.51.

2,7-Dichlorophenazine was prepared from 15.75 g p-nitrochlorobenzene, 12.8 g m-chloroaniline, 29 g pulverized KOH and 150 ml toluene. The solution in toluene was chromatogrammed. Yield 2.83 g (11.4%) base. Pale-yellow needles, m.p. 229-230° (from benzene).

Found %: N 11.33, 11.41; Cl 28.63, 28.59. $C_{12}H_6N_2Cl_2$. Calculated %: N 11.24; Cl 28.51.

10-(N)-oxide of 2,7-dichlorophenazine was obtained at the same time as the above base. Yield 0.61 g (2.5%). Crystallized from benzene as bright-yellow needles, m.p. 232-233° (with decomposition).

Found %: N 10.67, 10.71; Cl 26.55. $C_{12}H_6ON_2Cl_2$. Calculated %: N 10.57; Cl 26.79.

3,4-Dichloro-2'-nitrodiphenylamine was isolated during chromatogramming of the products in the preparation of 2,3-dichlorophenazine in amount of 4.3 g (7.5%). Red-orange needles from ligroine, m.p. 161-162°.

Found %: N 9.95, 10.10; Cl 24.85, 24.92. $C_{12}H_8O_2N_2Cl_2$. Calculated %: N 9.89; Cl 25.09.

The same compound was obtained by 20 hours' boiling of a mixture of 8.1 g 3,4-dichloroaniline, 7.9 g o-nitrochlorobenzene, 37 g nitrobenzene and 8.2 g potassium acetate. The nonreacted materials were distilled off in steam and the residue was recrystallized from aqueous alcohol. Yield 0.7 g (5%) red-orange needles, m.p. 158-159°. A mixed melting test with the preceding preparation did not give a depression.

3,4-Dichloro-4'-nitrodiphenylamine was isolated from the products in the synthesis of 2,3-dichlorophenazine. Yield 3.66 g (6.45%). Yellow-orange platelets from benzene, m.p. 214-215°.

Found %: N 10.08, 10.04; Cl 25.01, 25.11. $C_{12}H_8O_2N_2Cl_2$. Calculated %: N 9.89; Cl 25.09.

2,3-Dichloro-2'-nitrodiphenylamine was isolated from the products of condensation of 2.6 g 2,3-dichloroaniline, 6.85 g nitrobenzene and 95 g KOH powder in 30 ml toluene. 0.22 g (4.9%) orange-red needles from alcohol, m.p. 147-148°.

Found %: N 10.05, 9.79; Cl 24.85, 24.97. $C_{12}H_8O_2N_2Cl_2$. Calculated %: N 9.89; Cl 25.09.

2,3-Dichloro-4'-nitrodiphenylamine was isolated at the same time as the preceding preparation by chromatogramming from dichloroethane. 0.46 g (10.2%), bright-yellow needles from alcohol, m.p. 156-157°.

Found %: N 9.99, 10.13; Cl 25.09, 24.90. $C_{12}H_8O_2N_2Cl_2$. Calculated %: N 9.89; Cl 25.09.

SUMMARY

5 new bases were prepared by alkaline condensation of aromatic amines with nitro compounds: 1,2-, 1,3-, 1,4-, 2,3-, and 2,7-dichlorophenazines. The following N-oxides were isolated at the same time: 10-(N)-oxide of 1,2-dichlorophenazine, 10-(N)-oxide of 1,3-dichlorophenazine and 10-(N)-oxide of 2,7-dichlorophenazine.

Secondary and intermediate products of alkaline condensation which were isolated were 2,3- and 3,4-dichloro-2'-nitrodiphenylamines and 2,3- and 3,4-dichloro-4'-nitrodiphenylamines.

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CONFIGURATION AND PROPERTIES

OF UNSATURATED ACIDS AND THEIR DERIVATIVES

THE OXIDATION OF OCTADECENOIC ACIDS AND THEIR ESTERS

A. K. Plisov and N. P. Bulatsky

The structure of oleic acid was established by E. E. Vagner and was later confirmed by Baruch, although in contemporary literature, both at home and abroad, Baruch is credited with being the first to establish the correct formula of oleic acid [1]. However, this claim, which is accepted at the present time, does not correspond to reality. Actually, the first scientist who proposed the modern formula for oleic acid, in 1888, was the outstanding Russian chemist, Egor Egorovich Vagner [2]. Six years later, in 1894, Baruch [3] repeated the conclusions of E. E. Vagner and published his paper in the same journal in which Vagner's paper had appeared.

Concerning the spatial configuration of oleic acid, one of us has reported the data obtained on hydrogenation and oxidation of the geometrically isomeric octadecenoic acids [4]. Later Plisov and Maleeva studied the oxidation of oleic and elaidic acids with aqueous potassium permanganate [5] and showed that oleic and elaidic acids were oxidized at different velocities. Plisov and Bykovets made similar observations in respect of petroselinic and petroselaidic acids and their esters [10].

In these researches the reaction was performed at the surface between the acid or ester and an aqueous solution of the oxidizing agent. We considered that it was also necessary to clarify the nature of this reaction in a homogeneous medium.

We selected potassium permanganate as the oxidizing agent; it was used for the first time for the oxidation of oleic acid by Zaitsev [6]. The mechanism of this reaction which has been studied by Russian chemists [7, 8], was clarified by Nametkin [9] and is considered to involve addition of the potassium permanganate at the double bond with formation of an unstable intermediate product:

$$\begin{array}{l} H-C-OMnO_2OK \\ | \\ H-C-OMnO_2OK \end{array}$$

We must assume that the spatial conditions at the trans-compound will to some extent hinder the formation of the indicated intermed ate product.

As the solvent for this reaction, we selected acetone. This is convenient because after preliminary treatment with potassium permanganate, the acetone is oxidized extremely slowly; furthermore, we found that oxidation in acetone solution proceeds very much more slowly than in other solvents. This circumstance greatly facilitates the observations of changes in the rate of oxidation of oleic acid.

Since the blocking action of radicals at carbons linked by a double bond (steric hindrance) will mainly affect the first stage of the reaction (addition at the double bond), we decided to employ the oxidant in smaller quantities than are necessary for addition at the double bond, and to use weak solutions of oxidant.

Below are set forth the results of oxidation with potassium permanganate in acetone solution of oleic, elaidic, petroselinic and petroselaidic acids. As had been expected, the results demonstrate that the reactivity of these acids is consistent with the hypothesis of steric hindrance of the reactions, and they may serve as a basis for solution by a chemical method of the problem of the actual configuration of geometrically isomeric unsaturated acids.

EXPERIMENTAL

Pure oleic (9,10-octadecenoic) acid was obtained from commercial oleic acid via the lithium salts and had the following constants: b.p. 202° (5 mm); m.p. 14.4°; iodine number (Hübl) 90.04.

Elaidic acid was prepared by elaidinization of oleic acid and had the following constants after three recrystallizations from ethyl alcohol: b.p. 204° (5 mm); m.p. 51°; iodine number (Hübl) 89.96.

Petroselinic (6,7-octadecenoic) acid with m.p. 32.5° and iodine number 90.0 was isolated from coriander oil; its geometrical isomer (petroselaidic acid) was prepared by isomerization of petroselinic acid in presence of selenium and had, after recrystallization, m.p. 54° and iodine number 90.1.

The oxidation reaction was studied in a water thermostat in which the temperature could be kept constant to ± 0.05°. Comparable results were ensured by using identical weights of the acids concerned in two small flasks. To these was added acetone in quantity required to give a total volume of 2 ml in each flask (i.e., acid + acetone). The flasks were placed in the thermostat and after they had reached the temperature of the thermostat, addition was made of 48 ml oxidant solution. At specific intervals of time, 5 ml samples were withdrawn and the amount of unreacted oxidant was determined by titration of the reaction mixture with 0.04 N thiosulfate solution. Each experiment was repeated twice; the titration results varied by 0.02-0.04 ml.

TABLE 1

Experimental temperature 20°. Weight of acids 0.3115 g
Initial concentration of oxidant 0.04102 N.

Duration of oxidation (in minutes)	Amount of thiosulfate (in ml)			
	oleic acid	petroselinic acid	elaidic acid	petroselaidic acid
0	8.2	8.2	8.2	8.2
15	6.4	6.4	7.0	7.4
30	4.8	4.7	5.8	5.9
45	3.5	3.6	4.4	4.6
60	2.2	2.1	3.2	3.4
75	1.2	1.2	2.0	2.3
90	0.3	0.4	0.8	1.2

TABLE 2

Experimental temperature 10°. Weight of acids 0.3115 g
Initial concentration of oxidant 0.04102 N.

Duration of oxidation (in minutes)	Amount of thiosulfate (in ml)			
	oleic acid	petroselinic acid	elaidic acid	petroselaidic acid
0	8.2	8.2	8.2	8.2
30	6.7	6.7	7.3	7.4
60	5.4	5.3	6.4	6.8
90	4.2	4.4	5.4	5.9
120	3.2	3.4	4.3	4.8
150	1.9	1.9	3.4	4.0
180	0.5	0.6	2.5	3.0

TABLE 3

Experimental temperature 20°. Weight of acids 0.156 g.
Initial concentration of oxidant 0.04386 N.

Duration of oxidation (in minutes)	Amount of thiosulfate (in ml)			
	oleic acid	petroselinic acid	elaidic acid	petroselaidic acid
0	10.2	10.2	10.2	10.2
15	8.2	8.2	8.8	8.5
30	6.6	6.4	7.0	7.4
45	5.4	5.5	5.9	5.9
60	4.6	4.8	5.0	5.2
75	3.4	3.5	4.1	4.4
90	2.8	2.6	3.4	4.2

Since manganese dioxide is separated in the oxidation reaction and might obscure the titration data, we employed a method of sample withdrawal in vacuum which ensured manganese dioxide-free samples. For this purpose we used a tube to one end (the broad one) of which was attached a sintered porous plate. The required amount of reaction mixture was sucked into the tube with a pump and was filtered from manganese dioxide during this operation.

SUMMARY

1. Oleic and petroselinic acids are oxidized by potassium permanganate in acetone solution more rapidly than elaidic and petroselaidic acids.

2. Oxidation of octadecenoic acids with potassium permanganate in acetone solution proceeds as would be expected from the theory of steric hindrance.

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• See Consultants Bureau Translation, page 69.
•• " " " " " 637.

QUINONES

V. CHLORINATION OF 2,5-DIMETHOXYQUINONE

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In continuation of previously described work [1] on the chlorination of methoxyquinone, we decided to study the chlorination of 2,5-dimethoxyquinone (I). The sole chloro derivative described in the literature, 3,6-dichloro-2,5-dimethoxyquinone (II), was prepared not by direct chlorination of dimethoxyquinone but indirectly either by methoxylation of tetrachloroquinone [2] or by methylation of potassium chloranilate [3].

2,5-Dimethoxyquinone dissolves readily only in heated nitrobenzene. In our first experiments, therefore, we passed chlorine through a nitrobenzene solution of 2,5-dimethoxyquinone heated on a boiling water bath. After driving off the solvent in vacuum and recrystallizing the residue from alcohol, we obtained the reaction product in the form of bright orange-red plates with m.p. 142°. This substance was found to be identical with the above-noted 3,6-dichloro-2,5-dimethoxyquinone.

Subsequently, we carried out the reaction of chlorine with 2,5-dimethoxyquinone in milder conditions, the stream of dry chlorine being passed through a cooled suspension of the quinone in chloroform. Although 2,5-dimethoxyquinone is insoluble in chloroform, with continued passage of chlorine it dissolves. By observing a series of precautions, using thoroughly dried chloroform and chlorine, we obtained an almost completely colorless solution containing —as further examination revealed —previously undescribed products of addition of chlorine to 2,5-dimethoxyquinone in the form of 2,5-dimethoxyquinone dichloride (III) and 2,5-dimethoxyquinone tetrachloride (IV).

In order to obtain 2,5-dimethoxyquinone dichloride, it is best to conduct the reaction so that a little of the original quinone remains in the reaction medium. If this procedure is not followed, 2,5-dimethoxyquinone dichloride is extremely difficult to purify from tetrachloride and its accompanying secondary products, which form a resinous oil in the mixture; it is easily freed from unreacted 2,5-dimethoxyquinone by filtration. 2,5-Dimethoxyquinone dichloride crystallizes from ligroine in colorless needles melting at 145° (with decomposition).

In order to obtain 2,5-dimethoxyquinone tetrachloride, which generally has poor stability, it is best to start from previously isolated dichloride; chlorine is passed through a cooled solution of the latter in chloroform. The tetrachloride is then obtained in the solid state and is purified by crystallization from ligroine; the resultant crystals are unstable when heated and melt with decomposition.

When studying the properties of methoxyquinone dichloride [1], it was established that the presence of the methoxy group lowers the stability of the corresponding quinone chlorides. This observation was confirmed in a study of the properties of 2,5-dimethoxyquinone dichloride (III) and tetrachloride (IV). Both of these compounds also have poor stability and readily lose hydrogen chloride to form the corresponding chloro derivatives of 2,5-dimethoxyquinone.

From the dichloride (II) is also obtained the undescribed 3-chloro-2,5-dimethoxyquinone (V), while the tetrachloride (IV) gives the already known 3,6-dichloro-2,5-dimethoxyquinone (II). 2,5-Dimethoxyquinone tetrachloride slowly loses hydrogen chloride even on keeping or on solution in alcohol without heating. Both chlorides quickly split off hydrogen chloride when melted; the most convenient way of transforming 2,5-dimethoxyquinone chlorides into the corresponding chloro derivatives of 2,5-dimethoxyquinone is by short-period heating of their alcoholic solutions. On cooling the latter, the chloro derivatives come down in the pure form: 3-chloro-2,5-dimethoxyquinone (V) in the form of light-yellow needles with m.p. 118-119°, and 3,6-dichloro-2,5-dimethoxyquinone (II) in the form of orange-red platelets with m.p. 142°. The difference between the crystals is so great that these substances can be readily distinguished by their outward appearance, especially

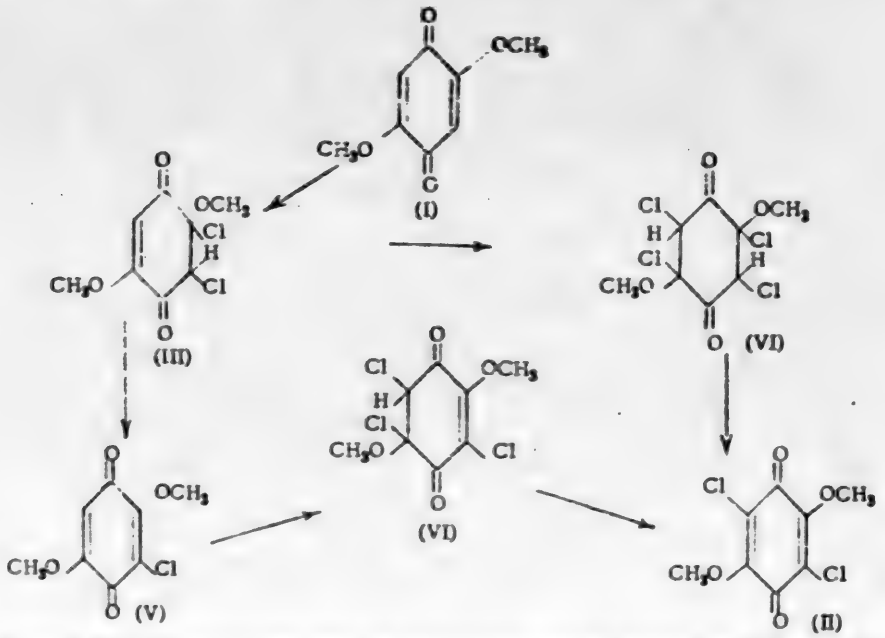
under the microscope. We exploited this difference in controlling the reaction during preparation of the tetrachloride.

3,6-Dichloro-2,5-dimethoxyquinone is rather less soluble in alcohol than the monochloro derivative. This difference can be utilized for the simultaneous preparation of both substances: a mixture of 2,5-dimethoxyquinone dichloride and tetrachloride is first prepared and then heated in alcohol; finally it is subjected to fractional crystallization.

3,6-Dichloro-2,5-dimethoxyquinone (II) was also prepared by us from previously isolated monochloro derivative (V), both directly and via the product of addition of chlorine to the latter, 3-chloro-2,5-dimethoxyquinone dichloride (VI). This compound is interesting because it contains one atom of chlorine replacing an atom of hydrogen and two atoms of chlorine added at the double bond of the quinoid nucleus. This addition product, obtained by passing chlorine through a solution of 3-chloro-2,5-dimethoxyquinone in chloroform, consisted of a light-colored oil which only solidified when cooled below −20°. This oil is soluble in boiling ligroine but on cooling, it separates out in the same form.

3-Chloro-2,5-dimethoxyquinone dichloride is extremely unstable and splits off hydrogen chloride even when kept. For this reason analytical determinations of the chlorine gave rather low results compared with the theoretical value. In alcoholic solution, especially when heated, the compound readily changes into 3,6-dichloro-2,5-dimethoxyquinone (II).

The transformations of the products of interaction of 2,5-dimethoxyquinone with chlorine which we studied are represented in the following scheme:



We prepared the 2,5-dimethoxyquinone for this investigation by Bückel's method [4], by heating p-benzoquinone with methyl alcohol in presence of zinc chloride. This reaction proceeds very smoothly, but the yield of 2,5-dimethoxyquinone reaches only 33% of the theoretical, reckoned on the quinone brought into reaction. According to Bückel, this low yield is due to initial formation of a product of addition of methyl alcohol to the quinone which rearranges into the corresponding methoxyhydroquinone and is oxidized by the quinone present to methoxyquinone.

The mechanism of this reaction has not yet been studied. It may be conjectured that it proceeds in several stages with intermediate formation of methoxyquinone, followed by an analogous transformation of the latter into 2,5-dimethoxyquinone. On this basis we hoped to raise the yield of 2,5-dimethoxyquinone by starting from previously prepared methoxyquinone. However, on heating methoxyquinone with methyl alcohol in presence of zinc chloride, we obtained no 2,5-dimethoxyquinone at all. It was found that in these conditions, under the influence of acid (formed by hydrolysis of the zinc chloride), the methoxyquinone undergoes transformation with formation

of the product of condensation of two molecules described in the preceding communication. It follows from this that methoxyquinone cannot be regarded as an intermediate product in the preparation of 2,5-dimethoxyquinone by Bückel's reaction. It is more probable, as was suggested by the author himself, that in this reaction, more rapid formation occurs (according to the usual mechanism for quinones) of the product of addition of 2 molecules of methyl alcohol to a molecule of quinone, and this is oxidized to 2,5-dimethoxyquinone with excess of quinone. If this hypothesis is correct, then the formation of 1 molecule of 2,5-dimethoxyquinone would actually require 3 molecules of quinone and the yield of 2,5-dimethoxyquinone cannot exceed 33% of the theoretical. Since the dimethoxyquinone is completely insoluble in alcohol, it is continuously precipitated as formed.

We hoped to raise the yield of 2,5-dimethoxyquinone by adding to the solution various oxidants such as iron chloride or nitric acid. But in such cases the yield was actually lowered, probably due to breakdown of the addition product formed.

We also prepared 2,5-dimethoxyquinone by treatment with methanol of monochloroquinone in presence of zinc chloride. In such a case direct methoxylation is accompanied by unusually easy removal of the chlorine atom of the other methoxy group. This behavior confirms the above-described mechanism of the reaction. In the case, however, of the chloroquinone in the intermediately formed addition product, clea. age of hydrogen chloride and oxidation are possible at the same time.

EXPERIMENTAL

1) Dimethoxyquinone Dichloride

6 g 2,5-dimethoxyquinone is finely pulverized and brought into 80 ml dry chloroform. A stream of dry chlorine is passed through the suspension until nearly the whole of the dimethoxyquinone has entered into reaction and gone into solution It is desirable to stop the flow of chlorine when there is still a little of the original quinone, since otherwise the tetrachloride is also formed. The resultant light-yellow solution is evaporated to a small bulk in vacuum. White crystals come down in the yellow oil. These are filtered, well pressed to remove oil, and washed with a little chloroform. The chloroform filtrate is diluted with ligroine, the precipitate is added to the main mass and the mixture is washed on the filter with ligroine.

The precipitate is purified by introducing it in small portions into boiling ligroine and then cooling the saturated solution. The resultant white crystals are filtered from the still-warm suspension. The whole of this operation must be performed quickly with avoidance of prolonged heating and prolonged standing of the solution. By adhering to these conditions, the reaction product is obtained in the pure form and is finally purified by one more recrystallization from ligroine. The yield of this product is about 4 g. Colorless, transparent needles melting at 145° (with decomposition). When heated with alcohol it splits off hydrogen chloride and forms 3-chloro-2,5-dimethoxyquinone. It is relatively stable when heated in ligroine.

0.1190 g sub.: 0.1416 g AgCl. 0.1261 g sub.: 0.1505 g AgCl. 0.1431 g sub.: 0.2807 g AgI. 0.1360 g sub.: 0.2688 g AgI. Found %: Cl 29.46, 29.52; OCH_3 25.87; 25.92. $C_6H_2O_2Cl_2(OCH_3)_2$. Calculated %: Cl 29.57; OCH_3 25.98.

2 Dimethoxyquinone Tetrachloride

2 g dimethoxyquinone dichloride is dissolved in 20 ml dry chloroform and a stream of chlorine is passed through the solution until a sample is found completely free from the original dichloride. The test is performed in the following manner: A few drops of solution are withdrawn from the reaction medium and put into 2 ml pure alcohol. The solution is brought to the boil and then cooled: the precipitate is transferred to the object glass of a microscope. The presence of long, acicular crystals of 3-chloro-2,5-dimethoxyquinone is evidence of the presence in the reaction medium of dichloride which has not yet entered into reaction. In the absence of the latter, only orange plates of 3,6-dichloro-2,5-dimethoxyquinone will be visible under the microscope; the latter is formed from the quinone tetrachloride.

When the test shows complete absence from the reaction medium of the original dichloride, the chloroform is distilled off in vacuum and the precipitate is washed with a little chloroform to remove the impurity in the form of a white mass. The crystaline precipitate is crystallized from ligroine with observance of the same precautions as for the crystallization of the dichloride.

Colorless crystals melting with decomposition. Dimethoxyquinone tetrachloride is less stable than the dichloride. On standing it slowly loses hydrogen chloride and is transformed into 3,6-dichloro-2,5-dimethoxyquinone. This transformation takes place very rapidly when the tetrachloride is put into boiling alcohol.

0.1362 g sub.: 0.2504 g AgCl. 0.1215 g sub.: 0.2238 g AgCl. 0.1574 g sub.: 0.2357 g AgI. 0.1214 g sub:

0.1835 g AgI. Found %: Cl 45.54, 45.61; OCH_3 19.74, 19.88. $C_6H_2O_2Cl_4(OCH_3)_2$. Calculated %: Cl 45.80; OCH_3 20.00.

3. 3-Chloro-2,5-dimethoxyquinone

3 g 2,5-dimethoxyquinone dichloride in small portions is introduced into 40 ml alcohol heated to the boil and the solution is boiled for 15 minutes. The reaction proceeds with evolution of hydrogen chloride. The solution gradually turns yellow and after cooling deposits light-yellow crystals of 3-chloro-2,5-dimethoxyquinone, which is purified by repeated crystallization from alcohol. Yield 3 g or 80% of the theoretically possible. Long light-yellow needles, m.p. 118-119°. Very slightly soluble in water; soluble in alcohol, ether, chloroform, gasoline and hot ligroine.

0.1198 g sub.: 0.0861 g AgCl. 0.1532 g sub.: 0.1090 g AgCl. 0.1004 g sub.: 0.2327 g AgI. 0.1384 g sub.: 0.3220 g AgI. Found %: Cl 17.79, 17.58; OCH_3 30.77, 30.72. $C_6HO_2Cl(OCH_3)_2$. Calculated %: Cl 17.53; OCH_3 30.62.

4. 3-Chloro-2,5-dimethoxyquinone Dichloride

3 g 3-chloro-2,5-dimethoxyquinone is dissolved in 30 g chloroform, the solution is cooled to 0°, and through it is passed chlorine until a test, similar to that described above for the preparation of 2,5-dimethoxyquinone tetrachloride, shows the complete absence of the original monochloro derivative from the reaction medium. The chloroform is then distilled off in vacuum and the residual yellow oil dissolved in boiling ligroine. On cooling, the reaction product separates in the form of heavy, oily drops which could not be crystallized after further purification. It only solidifies when cooled below −20°, but at 0° it again becomes oily. The color of the oil is light-yellow. On keeping, it slowly splits off hydrogen chloride and is transformed into 3,6-dichloro-2,5-dimethoxyquinone. In hot alcohol it quickly loses hydrogen chloride. It partly decomposes also when purified from ligroine and the chlorine content is, therefore, slightly lower than the theoretical value.

0.1542 g sub.: 0.2338 g AgCl. 0.1643 g sub.: 0.2512 g AgCl. Found %: Cl 37.52, 37.80. $C_8H_7O_2Cl_3$. Calculated %: Cl 38.93.

5. 3,6-Dichloro-2,5-dimethoxyquinone

a) 6 g 2,5-dimethoxyquinone is stirred into 60 ml nitrobenzene and the mixture is heated on a boiling water bath. Through this heated solution is passed a stream of dry chlorine for 2 hours. At the conclusion of the reaction, the nitrobenzene is taken off in vacuum and the dry residue crystallized from alcohol. Yield 6 g or 80% of the theoretical.

b) 3 g dimethoxyquinone tetrachloride is introduced into 40 ml boiling alcohol and boiling is continued for 15 minutes. The reaction is accompanied by evolution of hydrogen chloride. On cooling, the orange-yellow solution deposits crystals of 3,6-dichloro-2,5-dimethoxyquinone.

c) 3,6-Dichloro-2,5-dimethoxyquinone can also be obtained from the crude product of exhaustive addition of chlorine to 2,5-dimethoxyquinone, or from 3-chloro-2,5-dimethoxyquinone chloride, or from the resinous mass remaining on crystallization of 2,5-dimethoxyquinone dichloride.

The product is in the form of bright orange-red plates with m.p. 142°; insoluble in water, soluble in alcohol and ether. Readily crystallizes from ligroine. Is less soluble than the monochloro derivative in alcohol, and this difference can be utilized for separation from the latter by fractional crystallization.

0.1262 g sub.: 0.1540 g AgCl. 0.1416 g sub.: 0.1710 g AgCl. 0.1266 g sub.: 0.2486 g AgI. 0.1152 g sub.: 0.2283 g AgI. Found %: Cl 30.21, 29.92; OCH_3 25.95, 26.21. $C_6O_2Cl_2(OCH_3)_2$. Calculated %: Cl 29.96; OCH_3 26.16.

SUMMARY

Passage of chlorine through a solution of 2,5-dimethoxquinone in chloroform leads to 2,5-dimethoxyquinone dichloride and 2,5-dimethoxyquinone tetrachloride. Both these compounds have poor stability and lose hydrogen chloride readily with formation, respectively, of 3-chloro-2,5-dimethoxyquinone and 3,6-dichloro-2,5-dimethoxyquinone.

From 3-chloro-2,5-dimethoxyquinone was obtained 3-chloro-2,5-dimethoxyquinone dichloride which, by cleavage of HCl is also transformed into 3,6-dichloro-2,5-dimethoxyquinone.

3,6-Dichloro-2,5-dimethoxyquinone may also be obtained directly from 2,5-dimethoxyquinone by chlorination in heated nitrobenzene solution.

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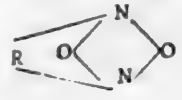
NAPHTHOFUROXAN

I. THE BISULFITE COMPOUND OF NAPHTHOFUROXAN

S. V. Bogdanov and B. I. Karavaev

As we know, oxidants act on the dioximes of o-quinones to form compounds with the general formula $R = N_2O_2$. These compounds are also obtained by oxidation of the corresponding o-nitroamino compounds or by decomposition of o-nitroazido compounds. These substances were formerly believed to have the structure of o-dinitroso compounds or of peroxides. Nowadays they are represented as oxides of furazines or as furoxans:

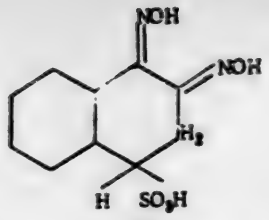
As evidence of the quinoid structure of these compounds, Hammick and others [1] adduce the addition of 4 atoms of bromine to benzofuroxan. The existence of two different products of oxidation of the amphi-dioximes of asymmetrical α-diketones, corresponding to the formulas of Meisenheimer and others [2], makes probable an asymmetrical configuration of the furoxan ring. Green and Rowe [4], who studied the oxidation of o-nitroanilines to the corresponding furoxans, at first proposed an asymmetrical formula for the latter and assumed that the nitrogen atom linked to the two oxygen atoms is located at the carbon previously linked with the nitro group. They later found, however, that oxidation of 4-chloro- and 5-chloro-2-nitroanilines leads to one and the same chlorobenzofuroxan [4]. A similar phenomenon is observed in the oxidation of 3-nitro-4-amino- or 4-nitro-3-aminotoluene and in the decomposition of 4- or 5-bromo-2-nitro-1-azidobenzene and 3-nitro-4-azido- or 4-nitro-3-azidotoluene [5]. Moreover, on oxidation of 2-nitro-1-naphthylamine and 1-nitro-2-naphthylamine and on decomposition of 2-nitro-1-azidonaphthalene or 1-nitro-2-azidonaphthalene, there is formed one and the same naphthofuroxan [6]. These facts led Green and Rowe to the conclusion that the furoxan group has the symmetrical structure



Although the attempt of Hammick and co-workers to establish the structure of furoxans by determination of the parachors of benzo- and methylbenzofuroxans did not lead to a decisive solution of the problem, they assumed an asymmetrical structure of furoxans. In their opinion, the formation of identical furoxans on oxidation of 4- or 5-substituted 2-nitroanilines is explained by the transition of the less stable furoxan isomer into the symmetrical o-dinitro form, followed by transformation into the stable isomer.

As previously pointed out [7], the sulfite compound of 1,2-naphthoquinone dioxime (I), which is obtained by the action of hydroxylamine on the bisulfite compound of 1-nitroso-2-naphthol, is converted by oxidation in an acidic medium into a colorless, crystalline substance containing nitrogen and sulfur. The oxidation product remained unexamined but it was considered to be closely related to naphthofuroxan which was first prepared by Ilyinsky [8] by oxidation of 1,2-naphthoquinonedioxime. On resuming the study of some derivatives of 1-nitroso-2-naphthol, we repeated the experiments on oxidation of the sulfite of 1,2-naphthoquinonedioxime. Using nitric acid, nitrous acid and hydrogen peroxide, we obtained one and the same substance in which, judging by its reduction to 1,2-naphthylenediamine-4-sulfonic acid, the structure of the naphthalene ring is retained as well as the original position of the atoms of nitrogen and sulfur. We attributed to this compound the structure of the bisulfite compound of naphthofuroxan. Since no data are available about the linkages of the oxygen atoms in the nitrogen-containing naphthofuroxan ring, we consider it is expedient for the present to use the formula of Green and Rowe.

Some properties of the oxidation product will be described later, but here we describe its sodium, potassium, barium and benzidine salts.



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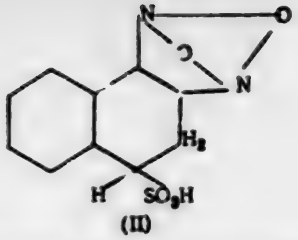

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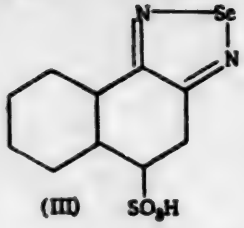

When preparing the initial sulfite compound of 1,2-naphthoquinonedioxime, it is unnecessary to boil the solution of the bisulfite compound of nitrosonaphthol with hydroxylamine (as indicated previously); the reaction already proceeds at room temperature, although much more slowly.

The structure of 1,2-naphthylenediamine-4-sulfonic acid was established by conversion with selenium dioxide into naphtho-selenoazole-sulfonic acid (III) and by comparison with the analogous product of transformation of the sulfonic acid prepared by cleavage of the azo compound formed from phenyldiazonium and 1-naphthylamine-4-sulfonic acid. In this case use was made with slight modification of Hinsberg's method [9] for the preparation of naphthoselenodiazole from 1,2-naphthylenediamine.

EXPERIMENTAL

Sulfite compound of 1,2-naphthoquinonedioxime was prepared by 30 minutes' boiling of a solution of the bisulfite compound of 1-nitroso-2-naphthol with a small excess of hydroxylamine hydrochloride and sodium acetate, followed by acidification of the cooled solution.

On standing a solution of 11.08 g of the bisulfite compound of 1-nitroso-2-naphthol, 6.56 g crystalline sodium acetate and 3.06 g hydroxylamine hydrochloride in 75 ml water at 18-20°, the reaction for 1-nitroso-2-naphthol disappeared after 48 hours. Acidification of the cooled solution with hydrochloric acid brought down 7 g of sulfite compound.

Oxidation of the Sulfite Compound

1. Nitric acid. To a solution of 10.8 g (0.04 mole) sulfite compound and 2.2 g crystalline sodium carbonate in 100 ml water was added 42.5 ml 59.4% nitric acid; the mixture was heated to 90-95° and kept at this temperature for 50 minutes. Already at 50° the evolution of oxides of nitrogen commenced and subsequently the odor of naphthofurazan was detected. Into the cooled and filtered solution was introduced 21 g crystalline sodium carbonate; the resultant precipitate was filtered and washed with water and alcohol. Yield 9.8 g.

The reaction may be so conducted that the stage of separation of sulfite compound is avoided. The paste of nitrosonaphthol, obtained in the usual way from 0.2 mole 2-naphthol, was washed until neutral and expressed; it was then dissolved in 57.4 g 36.2% sodium bisulfite diluted with an equal amount of water. Into the filtered solution was introduced 38 g crystalline sodium acetate and 16.8 g hydroxylamine hydrochloride; the solution was boiled for 30 minutes and filtered. After dilution to 260 ml, the filtrate was run over a period of $^1/_2$ hour into a heated (65-68°) solution of 164 ml 56.5% nitric acid in 200 ml water. The mixture was heated to 90°, kept at this temperature for 15 minutes and filtered. To the filtrate was added sodium chloride (20 g per 100 ml filtrate); the precipitated sodium salt of the oxidation product was filtered and washed with water and methyl alcohol. Yield 50.6 g (74% of theory on the 2-naphthol).

2. Nitrous acid. Into 90 ml solution of the bisulfite compound of 1,2-naphthoquinonedioxime, prepared from 0.1 mole 2-naphthol, was introduced 8 g sodium bicarbonate and 20.7 g sodium nitrite; the solution was run in the course of 35 minutes into a heated (30-40°) mixture of 40 ml 35.4% hydrochloric acid and 100 ml water. The suspension formed was heated to 95° and held at this temperature for 15 minutes. The solution was filtered and cooled. The precipitate was filtered and washed with water and methyl alcohol. Yield 19.0 g. Partial concentration of the filtrate led to separation of an additional 2.6 g substance.

3. Hydrogen peroxide. Into a boiling suspension of 5.4 g sulfite compound of 1,2-naphthoquinonedioxime in a mixture of 20 ml 35.4% hydrochloric acid and 40 ml water was run dropwise 30 ml 30% hydrogen peroxide. Fairly rapid formation occurred of a light-yellow solution containing an insignificant amount of resinous particles; the odor of chlorine was detected. The filtered and cooled solution was partly neutralized with sodium carbonate and the precipitate was filtered and washed with alcohol. Yield 2.5 g. The substance did not contain chlorine.

The same result was obtained by substituting sulfuric acid for hydrochloric acid.

The sodium salt of the product of oxidation was purified by crystallization from double the amount of water or by precipitation from an aqueous solution of alcohol. Colorless rectangular plates. Relatively stable in acid solutions, but boiling in 30-69% sulfuric acid resulted in browning and formation of naphthofurazan (m.p. 78°).

The compound contains 3 molecules of water of crystallization, $2^1/_4$ of which are driven off at 140°; at a higher temperature the compound decomposes.

0.1705 g sub.: 0.0352 g Na_2SO_4. 0.1416 g sub.: 10.2 ml N_2 (17°, 747 mm). Found %: Na 6.69; N 8.33. $C_{10}H_7O_5N_2SNa \cdot 3H_2O$. Calculated %: Na 6.69; N 8.14.

The potassium salt was prepared from the sodium salt. Colorless rectangular plates, fairly readily soluble in cold water, insoluble in alcohol.

1.1034 g sub.: loss on drying (130°) 0.0618 g. 0.0924 g sub.: 7.2 ml N_2 (21.5°, 729 mm). 0.2354 g dry sub.: 0.0648 g K_2SO_4. Found %: H_2O 5.60; N 8.66; K 12.35. $C_{10}H_7O_5N_2SK \cdot H_2O$. Calculated %: H_2O 5.55; N 8.64. $C_{10}H_7O_5N_2SK$. Calculated %: K 12.77.

The barium salt was prepared from the sodium salt. Colorless elongated plates with pointed ends; poorly soluble in cold and fairly soluble in hot water.

0.6954 g sub.: loss on drying (130°) 0.0914 g. 0.1275 g sub.: 0.0386 g $BaSO_4$. 0.0940 g sub.: 5.3 ml N_2 (20°, 748 mm). Found %: H_2O 13.12; Ba 17.81; N 7.68. $(C_{10}H_7O_5N_2S)_2Ba \cdot 5.5H_2O$. Calculated %: H_2O 12.85; Ba 17.82; N 7.27.

The benzidine salt was prepared from the sodium salt and benzidine hydrochloride. Colorless elongated plates, poorly soluble in cold and fairly soluble in hot water, insoluble in alcohol.

0.6132 g sub.: loss on drying (120°) 0.0290 g. 0.7374 g sub.: 19.71 ml 0.1 N $NaNO_2$. Found %: H_2O 4.72; M 748. $(C_{10}H_8O_5N_2S)_2C_{12}H_{12}N_2 \cdot 2H_2O$. Calculated %: H_2O 4.76; M 756.

1,2-Naphthylenediamine-4-sulfonic acid

1) To a solution of 20.6 g sodium salt of the bisulfite compound in 120 ml water is run in 120 ml ammonia solution, followed gradually at 33-50° by 40 g zinc dust. After 7 hours' stirring at 60°, the mixture is filtered and the filtrate acidified with hydrochloric acid. The precipitate is filtered and washed with water. Yield 9.1 g.

2) Into a solution of 10.3 g sodium salt in 150 ml water is run 35 ml 40% NaOH, followed at 15-35° over a period of 45 minutes by 20 g zinc dust. After 20 minutes' stirring at 35°, the mixture is filtered and the filtrate acidified with hydrochloric acid. The light-brown precipitate (prisms) is filtered and washed with water. Yield 6.8 g.

After reprecipitation from sodium acetate solution, the substance has a faint brown tint. Oxidation with nitric acid converts it into 1,2-naphthoquinone-4-sulfonic acid (characterized by formation of red 1,2-naphthoquinone-4-anilide with aniline), and treatment with the bisulfite compound of phenanthrenequinone gives naphthophenanthrazine-sulfonic acid (yellow needles, soluble in sulfuric acid with a blue color).

Naphthoselenodiazole-sulfonic Acid

Into a suspension of 7.14 g naphthylenediamine-sulfonic acid in 15 ml water was run 7.0 g selenium dioxide at the normal temperature in a single portion. After brief stirring, a brown solution was obtained. Into the solution was run 20 ml 34% NaOH and the light-colored precipitate was filtered and washed with water and alcohol. Yield 10.27 g.

The substance crystallized from water in the form of colorless long prisms.

1.0440 g sub.: loss on drying (130°) 0.0663 g. 0.3134 g dry sub.: 0.0651 g Na_2SO_4. Found %: H_2O 6.35; Na 6.73. $C_{10}H_5O_3N_2SSeNa \cdot 1.25\ H_2O$. Calculated %: H_2O 6.29. $C_{10}H_5O_3N_2SSeNa$. Calculated %: Na 6.86.

The sulfochloride was obtained by 48 hours' standing of a mixture of the sodium salt of the sulfonic acid with an equal amount of phosphorus pentachloride at the ordinary temperature and was separated by diluting the mixture with ice. Yellowish bipyramids (from chlorobenzene), m.p. 204.5-205.3°.

1,2-Naphthylenediamine-4-sulfonic acid, prepared by decomposition of the azo compound from phenyldiazonium and 1-naphthylamine-4-sulfonic acid, possessed the same properties as the product of reduction of the bisulfite compound. The sodium salt of naphthoselenodiazole-sulfonic acid was prepared as above.

1.0352 g sub.: loss on drying (130°) 0.0361 g. 0.1682 g dry sub.: 0.0352 g Na_2SO_4. Found %: H_2O 6.39; Na 6.78.

The sulfochloride had m.p. 205.5-206°; a mixture of both sulfochlorides melted at 205-205.5°.

SUMMARY

1. Oxidation of the sulfite of 1,2-naphthoquinonedioxime with nitric acid, nitrous acid or hydrogen peroxide leads to the sulfite of naphthofuroxan. The sodium, potassium, barium and benzidine salts of the oxidation product were prepared.

2. Reduction of the bisulfite compound of naphthofuroxan with zinc in presence of ammonia or sodium hydroxide leads to 1,2-naphthylenediamine-4-sulfonic acid.

3. Oxidation of 1,2-naphthylenediamine-4-sulfonic acid with selenium dioxide leads to naphthoselenodiazolesulfonic acid.

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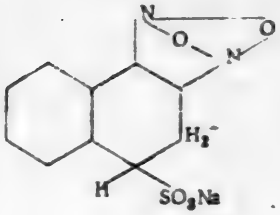
NAPHTHOFUROXAN

II. 2-NITRO-1-NAPHTHYLAMINO-4-SULFONIC ACID AND 2-NITRO-1-NAPHTHOL-4-SULFONIC ACID

S. V. Bogdanov and I. N. Koroleva

A method was previously described [1] for the preparation of the bisulfite compound of naphthofuroxan (I). This compound was found to be very unstable toward alkalies, the degree of sensitivity depending upon the conditions of use and the nature of the alkaline agent. Naphthofuroxan (II), the normal product of breakdown of the bisulfite compound, is formed only in minor amounts. Below is described the transformation of the bisulfite compound in presence of sodium carbonate.

Boiling of the bisulfite compound with sodium carbonate solution gives 2-nitro-1-naphthol-4-sulfonic acid (III), naphthofuroxan, naphthofurazan and a sulfonic acid of unknown structure, which contains nitrogen. In suitable conditions 2-nitro-1-naphthol-4-sulfonic acid is the main product of the reaction and is obtained in a yield of 93% of the theoretically possible. As experiments showed, the formation of this sulfonic acid proceeds via hydrolysis of the amino group in the initial reaction product —2-nitro-1-naphthylamine-4-sulfonic acid (IV). This amino compound is obtained by keeping the bisulfite compound in 1% sodium carbonate solution at the ordinary temperature; heating greatly accelerates the reaction; after 10 minutes' boiling of this mixture the yield of 2-nitro-1-naphthylamine-4-sulfonic acid reaches 89% of the theoretical. Formation of secondary reaction products is also observed in this case.



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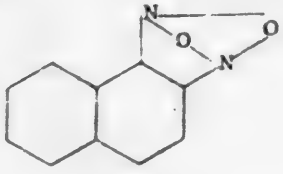

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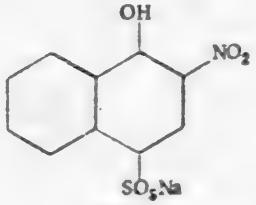

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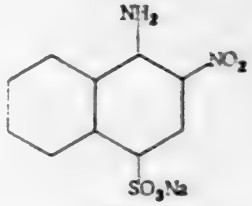

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Conversion of the bisulfite compound of naphthofuroxan into 2-nitro-1-naphthylamine-4-sulfonic acid is similar to some extent to the transformation of the bisulfite compound of 1-nitroso-2-naphthol into 1-amino-2-naphthol-4-sulfonic acid [2]. Naphthofuroxan is obtained as the result of normal decomposition of the bisulfite compound of naphthofuroxan, while the formation of naphthofurazan can be explained by reduction of naphthofuroxan and of the bisulfite compound of naphthofuroxan with the split-off sodium sulfite.

The structure of 2-nitro-1-naphthol-4-sulfonic acid was established by its conversion into 2,4-dinitro-1-naphthol, into 2-amino-1-naphthol-4-sulfonic acid and into 2-nitro-1-naphthol.

The structure of 2-nitro-1-naphthylamine-4-sulfonic acid, already inferred from its transformation into 2-nitro-1-naphthol-4-sulfonic acid, was confirmed by conversion into 1,2-naphthylenediamine-4-sulfonic acid and into 2-nitro-1-naphthylamine.

The diazo compound of 2-nitro-1-naphthylamine-4-sulfonic acid is obtained in normal conditions and possesses the normal azo-coupling ability; under the action of sodium carbonate, however, it loses the nitro group and is converted into the poorly active 1-diazo-2-naphthol-4-sulfonic acid.

EXPERIMENTAL

2-Nitro-1-naphthylamine-4-sulfonic Acid

1) Into a solution of 61.9 g (0.18 mole) sodium salt of the bisulfite compound of naphthofuroxan in 450 ml water is introduced at the ordinary temperature 4.5 g calcined sodium carbonate; the mixture is heated to the boil, and after 10 minutes' boiling it is cooled. The resultant very small yellowish precipitate is filtered off and to the

filtrate is added sodium chloride (20% of the volume). The precipitated orange platelets of the sodium salt of nitronaphthylamine-sulfonic acid are filtered and washed with water, methyl alcohol and ether. Yield 46.75 g (89.5% of theory).

The filtrate and residue after evaporation of the alcohol and ether, is boiled for an hour. After cooling, the yellowish filtrate is filtered and washed with water. Weight of precipitate 1.86 g (precipitate a).

The filtrate is acidified with 8.5 ml hydrochloric acid and the resultant yellow crystalline precipitate is filtered and washed. Weight of substance 4.23 g (precipitate b).

2) To a solution of 10.3 g sodium salt of the bisulfite compound in 200 ml water was added 23 g 9.5% sodium carbonate solution and the mixture left for 18 hours at 18-20°. Addition of sodium carbonate to the filtered solution brought down 4.71 g sodium salt of nitronaphthylamine-sulfonic acid; boiling of the filtrate gave 0.28 g precipitate a and 2.23 g precipitate b.

The sodium salt is readily soluble in water and much less soluble in ethyl alcohol. From water it crystallizes in the form of orange, long, slender platelets. Drying at 125° indicated the absence of water of crystallization.

0.0994 g sub.: 0.0236 g Na_2SO_4. Found %: Na 7.69. $C_{10}H_7O_5N_2SNa$. Calculated %: Na 7.93.

The potassium salt (prepared from the sodium salt) crystallizes from water as orange prisms.

1.0028 g sub.: loss on drying (120°) 0.0494 g. 0.2066 g dry sub.: 0.0570 g K_2SO_4. Found %: H_2O 4.93; K 12.38. $C_{10}H_7O_5N_2SK \cdot H_2O$. Calculated %: H_2O 5.55. $C_{10}H_7O_5N_2SK$. Calculated %: K 12.77.

1,2-Naphthylenediamine-4-sulfonic Acid

Into a solution of 11.6 g sodium salt of the amino compound in 200 ml water, acidified with 64 ml hydrochloric acid, is introduced at 65-90° over a period of 40 minutes 16 g zinc dust, and the mass is stirred at 90° for another 20 minutes. The precipitate is filtered and washed with water. The yield of diamino compound, after reprecipitation from sodium acetate solution, is 7.1 g; long, slender prisms. With the bisulfite compound of phenanthrenequinone the substance gives the yellow naphthophenanthrazine-sulfonic acid; with nitric acid it is oxidized to 1,2-naphthoquinone-4-sulfonic acid; with selenium dioxide it forms the corresponding selenodiazole whose sulfochloride melts at 204.5-205°.

2-Nitro-1-naphthylamine

A mixture of 20 g of the sodium salt of nitronaphthylamine-sulfonic acid and 600 ml 40% sulfuric acid was heated at 108-112° for 2 hours. The cooled suspension was run into 800 ml water and the yellow crystalline precipitate filtered and washed with water. In order to separate the unreacted sulfonic acid, the precipitate was heated to 90° with 200 ml water and 40 ml ammonia solution, the insoluble portion was filtered off and washed with 400 ml water at 95°. Yield of nitronaphthylamine 6.23 g. (From the filtrates from the nitronaphthylamine was isolated 7.94 g potassium salt of the original sulfonic acid by addition of potassium chloride.) Nitronaphthylamine crystallizes from methyl alcohol as orange prisms with m.p. 142.5-143°. Nitrous acid converts it into a yellow solution of diazo compound which, with 2-naphthol-3,6-disulfonic acid, forms a blue-red dye and with resorcinol a reddish-brown dye. After treatment with sodium carbonate, the diazo compound does not couple with 2-naphthol-3,6-disulfonic acid, but with resorcinol it gives a lilac dye.

1-Diazo-2-naphthol-4-sulfonic Acid

A solution of 5 g of the sodium salt of nitronaphthylamine-sulfonic acid and 1.31 g sodium nitrite in 100 ml water is run over a period of 30 minutes at 3-7° into 10 ml hydrochloric acid + 100 ml water; the resultant suspension of diazo compound is stirred for another $1\frac{1}{2}$ hours. The diazo compound (long, yellow prisms) gives, with 2-naphthol-3,6-disulfonic acid, a lilac dye, with resorcinol a brown dye, and with 2-naphthol-3,6-disulfonic acid a reddish-brown dye. To the suspension at 20° is added, over an hour, 8.5 g calcined sodium carbonate. The orange solution does not couple with the above-mentioned sulfonic acids, but with resorcinol it forms a deep lilac dye. The solution, after filtering from turbidity, is acidified with 25 ml hydrochloric acid. The precipitated diazonaphtholsulfonic acid (yellow prisms) is filtered and washed to give 3.48 g (79.6%) diazo compound (64.3% of the theoretical amount).

The above-noted precipitate a was only partly soluble in hot water. From the aqueous solution were separated colorless prisms of sodium salt of the sulfonic acid. The compound was free from water of crystallization and contained 8% sodium. Reduction with zinc and hydrochloric acid converted it into 1,2-naphthylenediamine-4-sulfonic acid. The examination of the substance was not completed.

Recrystallization of the water-insoluble portion from methyl alcohol gave a small amount of naphthofurazan with m.p. 78° and a substance with m.p. 123.5-124.5°. The mixture of the substance with the naphthofuroxan obtained by oxidation of 1,2-naphthoquinonedioxime with nitric acid (m.p. 124.6-125.5°) melted at 124.5-125.5°.

Precipitate b was the sodium salt of 2-nitro-1-naphthol-4-sulfonic acid.

2-Nitro-1-naphthol-4-sulfonic Acid

1) A solution of 10 g sodium salt of nitronaphthylamine-sulfonic acid in 100 ml 14.1% sodium carbonate was boiled for 2 hours. The reddish-orange solution was diluted with 60 ml water and acidified with 30 ml hydrochloric acid; the precipitated sodium salt of nitronaphthol-sulfonic acid was filtered and washed with water. Yield 9.4 g or 88.2% of the theoretical.

2) To a boiling solution of 32 g calcined sodium carbonate in 150 ml water was added, over an hour, a solution of 20.6 g sodium salt of the bisulfite compound of naphthofuroxan in 150 ml water, and the boiling was continued for a further 2 hours. In the reflux condenser separated needles of naphthofurazan, while cooling of the solution brought out a mixture of secondary products (1.1 g) containing the same components as in precipitate a obtained during preparation of nitronaphthylamine-sulfonic acid. The filtrate from the precipitated sodium salt of nitronaphthol-sulfonic acid was filtered and washed. Yield 17.3 g (93.3% of the theoretical).

If solutions of bisulfite compound and sodium carbonate are mixed at the ordinary temperature and then heated, the yield of nitronaphthol-sulfonic acid falls while the amount of secondary products increases.

The sodium salt is fairly soluble in water from which it crystallizes as yellow, slender platelets, difficultly soluble in alcohol.

1.0032 g sub.: loss on drying (125°) 0.0598 g. 0.0706 g dry sub.: 0.0168 g Na_2SO_4. Found %: H_2O 5.96; Na 7.70. $C_{10}H_6O_6NSNa \cdot H_2O$. Calculated %: H_2O 5.83. $C_{10}H_6O_6NSNa$. Calculated %: Na 7.90.

2-Amino-1-naphthol-4-sulfonic Acid

A solution of 4.4 g sodium salt of nitronaphthol-sulfonic acid in 150 ml water was boiled with a solution of tin chloride (150% excess) in hydrochloric acid for 20 minutes. The precipitate (long prisms) was filtered and washed. Yield 3.22 g.

A solution of the diazo compound gave a magenta-red coloration with resorcinol.

2.85 g amino compound was gradually brought at 5-10° into a mixture of 1.3 ml nitric acid (sp. gr. 1.35) and 3 ml water. The mass was diluted with water and to the filtered solution was added a saturated solution of potassium chloride; the precipitated potassium salt of 1,2-naphthoquinone-4-sulfonic acid was filtered; yield 2.36 g. Addition of an aqueous solution of aniline to the solution of potassium salt led to precipitation of 1,2-naphthoquinone-4-anilide. The compound crystallizes from alcohol in the form of small red needles, m.p. 257° (with decomposition).

2,4-Dinitro-1-naphthol

To a solution of 5 g nitronaphthol-sulfonic acid in 150 ml water was added 15 ml nitric acid (sp. gr. 1.35) and the mixture gradually heated to the boil. The dinitronaphthol formed was filtered and reprecipitated from sodium carbonate solution; yield 2.48 g. The compound crystallized from alcohol as yellow needles, m.p. 138.5° (with decomposition). (Formation of dinitronaphthol is facilitated by adding a small quantity of sodium nitrite to the solution of nitronaphthol-sulfonic acid.)

2-Nitro-1-naphthol

A mixture of 5 g nitronaphthol-sulfonic acid and 90 g 40% sulfuric acid was boiled for 7 hours. After only 30 minutes a sublimate of yellow needles of nitronaphthol had formed in the upper part of the flask. The mixture was diluted with water and the nitronaphthol filtered off; yield 2.1 g. The compound was reprecipitated from sodium carbonate solution and crystallized from methanol. Long yellow prisms, m.p. 128.5-129°.

SUMMARY

1. The main product of transformation of the bisulfite compound of naphthofuroxan in weak sodium carbonate solution at the ordinary temperature or after short-period boiling is 2-nitro-1-naphthylamine-4-sulfonic acid.

2. Prolonged boiling of the bisulfite compound with sodium carbonate solution leads mainly to formation of 2-nitro-1-naphthol-4-sulfonic acid.

3. Decomposition of the bisulfite compound of naphthofuroxan in sodium carbonate solution gives, apart from

2-nitro-1-naphthylamine-4-sulfonic acid and 2-nitro-1-naphthol-4-sulfonic acid, small amounts of naphthofuroxan and naphthofurazan.

4. The diazo compound of 2-nitro-1-naphthylamine-4-sulfonic acid is transformed by the action of sodium carbonate into 1-diazo-2-naphthol-4-sulfonic acid.

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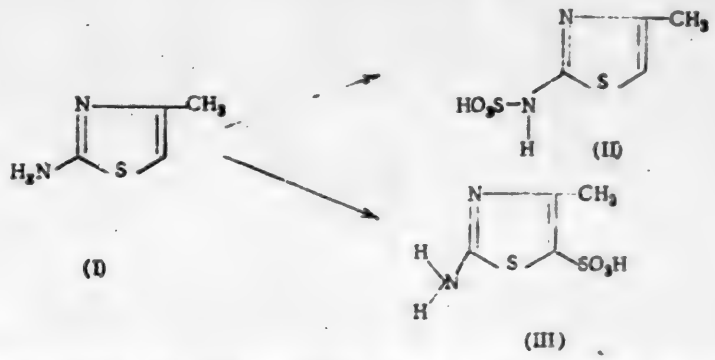
* See Consultants Bureau Translation, page 1855.

THE STRUCTURE OF THE SULFONIC ACIDS OF 2-AMINO-4-METHYLTHIAZOLE

I. Ya. Postovsky and T. S. Mamykina

On sulfonating 2-amino-4-methylthiazole (I), Ochiai and Nagasawa [1] obtained, depending on the reaction conditions, two isomeric acids: in the cold they obtained an acid with m.p. 256° (with decomposition), while with heating on the water bath they got an acid whose decomposition point was above 340°. The acid with m.p. 256° changes into the acid with decomposition point above 340° when heated with strong sulfuric acid. This transition of a low-melting sulfonic acid into a high-melting one is analogous to the known conversion of arylsulfamic acids into arylaminosulfonic acids. On this analogy, Ochiai and Nagasawa regarded the acid with m.p. 256° as a sulfamic acid and the one with m.p. above 340° as the 5-sulfonic acid.

In the present communication, we show that this argument "by analogy" is fallacious and that in the 2-aminothiazole series there occurs a characteristic transition in the reverse direction from the sulfonic acid (III) into the sulfamic acid (II).



(I) (II) (III)

We reached this conclusion on the basis of a repeated study of the structure of the sulfochloride and sulfamides of 2-acetamino-4-methylthiazole which we had previously described (IV) [2].

It was shown at the time that the action of chlorosulfonic acid on 2-acetamino-4-methylthiazole (IV) leads smoothly to the sulfochloride from which, by reaction with various amines, can be obtained a series of sulfamides. In order to establish the position of the sulfamido group, the starting sulfochloride was subjected to hydrolysis. This gave an acid with m.p. 253-255° (with decomposition) which, according to Ochiai and Nagasawa, should be regarded as the sulfamic acid. It was, therefore, concluded that in the chlorosulfonation of 2-acetamino-4-methylthiazole, the hydrogen of the acetamino group is substituted and that, consequently, the sulfamides are derivatives of the sulfamic acid (II).

Almost simultaneously with the publication of our paper in which these conclusions were announced, papers appeared by Backer and co-workers [3, 4] describing the sulfochloride of 2-acetamino-4-methylthiazole and the sulfamides prepared from this sulfochloride. The compounds described by Backer and co-workers, as far as can be judged from the melting points cited in the abstract of the paper [3], are identical with the compounds previously prepared by us. But Backer and co-workers regarded their compounds as derivatives of the sulfonic acid (III) without putting forward any experimental evidence in support of this assumption.

Two years later a detailed paper was published by Hurd and Kharasch [5] devoted to the structure of the sulfonic acids of Ochiai and Nagasawa. In it the authors arrived at the conclusion that the low-melting acid with m.p. 253° is the sulfamic acid, i.e., they supported the data of Ochiai and Nagasawa for the structure of the sulfonic acids of 2-amino-4-methylthiazole and their views on the isomerization of these acids.

Although in the paper of Hurd and Kharasch no strict proof is advanced for the structure of the sulfonic acids of 2-amino-4-methylthiazole, their arguments in some measure confirmed our conclusion about the structure of the sulfochloride and the sulfamides as derivatives of the sulfamic acids (II). Later Hurd and Wehrmaster [6], in a re-

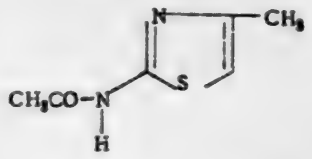
consideration of the structure of the sulfochloride, pointed out the correctness of our conclusions about the structure of the sulfochloride, based on the results of hydrolysis of the sulfochloride to the acid with m.p. 253°. However, all these data conflicted with the observations according to which substitutions in 2-acetylamino-4-methylthiazole proceed easily in the 5-position (for example, halogenation and other reactions) [1, 7].

For these reasons, a number of authors still consider the question of the structure of the sulfochloride to be an open one [8].

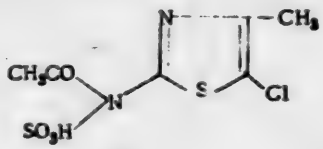
For the purpose of verifying our conclusions about the structure of the sulfochloride prepared by the action of chlorosulfonic acid on 2-acetamino-4-methylthiazole, we thought it would be expedient to carry out the reverse conversion of the acid with m.p. 253°, prepared by Hurd and Kharasch, into the sulfochloride.

The acid with m.p. 253°, prepared (according to Hurd and Kharasch) by the action of strong sulfuric acid on free 2-amino-4-methylthiazole in dichloroethane solution, was converted into the sodium salt and acetylated by heating with acetic anhydride. Reaction of the acetyl derivative with PCl_5 gave an acid chloride whose properties and melting point (mixed test) proved to be identical with those of the sulfochloride obtained by us by direct chlorosulfonation of the acetyl derivative of amine (IV). In this manner the circle was completed, so to speak, of the transformations, which confirmed our previously enunciated conclusions on the structure of the sulfochloride.

Nevertheless, as we shall see later, in these conclusions resides an error which could only be revealed in the course of another investigation, in which it was required to synthesize 5-chloro-substituted derivatives of the type of (V).



(IV)



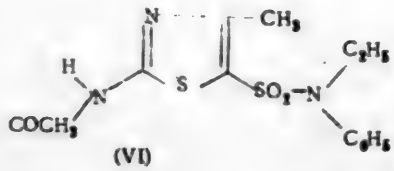
(V)

In order to obtain the starting material for the synthesis of these compounds, i.e., the chloro-substituted sulfochloride, we followed the method indicated in our preceding communication: action of chlorosulfonic acid on 2-acetamino-4-methyl-5-chlorothiazole. To our surprise, this compound did not enter into reaction with chlorosulfonic acid. The 5-bromo-derivative proved to be equally inert to chlorosulfonic acid. We, therefore, tried to prepare the required halogen derivative (V) by halogenating the sulfochloride of 2-acetamino-4-methylthiazole. However, the action of bromine in chloroform solution on the sulfochloride failed to give the anticipated bromo derivative and the sulfochloride was recovered unchanged. By contrast, in the same conditions 2-acetamino-4-methylthiazole, i.e., a compound without a substituent in the 5-position, is smoothly brominated with formation of the corresponding 5-bromo derivative.

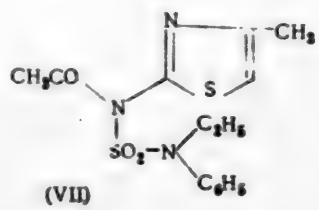
All this led up to the idea that, contrary to former conclusions, in the chlorosulfonation of 2-acetamino-4-methylthiazole it is not the hydrogen of the acetamino group but the hydrogen in the 5-position in the ring which is substituted. Only thus can we account for the failure to realize the halogenation of the sulfochloride or the sulfochlorination of 5-halogen-substituted derivatives.

The following experiments provided further proof of the accuracy of this conclusion.

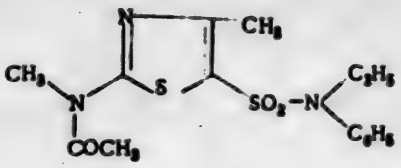
The action of ethylaniline on the sulfochloride of 2-acetamino-4-methylthiazole gave a disubstituted sulfamide. If the sulfochloride group is in the 5-position, then reaction with ethylaniline must give the amide of structure (VI), but if the sulfochloride group was located at the amino group, then a product of structure (VII) should have been formed.



(VI)

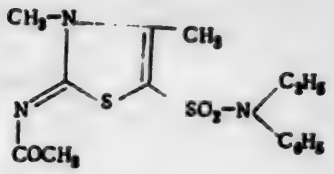


(VII)



(VIII)

or

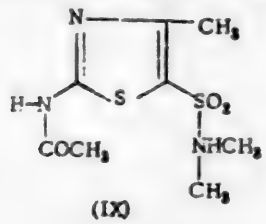


(VIIIa)

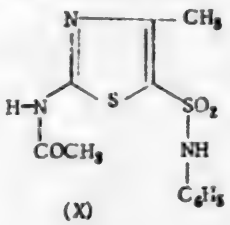
The substance with structure (VI) contains the acetamino group and should, therefore, like 2-acetamino-4-methylthiazole (IV), be soluble in caustic alkali and should be susceptible to methylation with dimethyl sulfate. But if the substance had structure (VII), then it should not dissolve in alkali and should not be methylated by dimethyl sulfate. Experiment showed that the disubstituted amide is readily soluble in caustic alkali and is smoothly methylated by dimethyl sulfate with formation in good yield of a product to which the structure of (VIII) or (VIIIa) can be ascribed. Consequently, we must assign structure (VI) to the starting substance.

Structure (VI) for the disubstituted amide is also confirmed by the fact that the product reacts with CH_3MgI, and on analysis by the Chugaev-Tserevitinov method loses 1 mole methane per mole of substance; product (VIII) naturally cannot react with an organomagnesium compound.

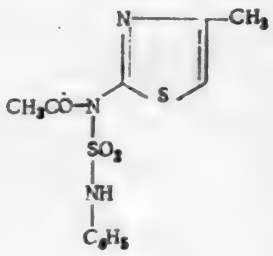
These observations were further strengthened by the determination of the active hydrogen content by the Chugaev-Tserevitinov method in the starting substance—2-acetamino-4-methylthiazole (IV)—as well as in the dimethylsulfamide (IX) and the sulfanilide (X) prepared from the sulfochloride. One active hydrogen was detected in 2-acetamino-4-methylthiazole (IV), and the same in the dimethylsulfamide (IX), thereby confirming their structure. The anilide was found, in agreement with structure (X), to have two active hydrogens. If the anilide had possessed structure (XI), then it would have contained only one active hydrogen.



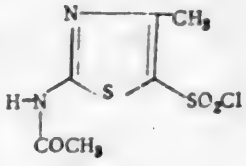
(IX)



(X)



(XI)



(XII)

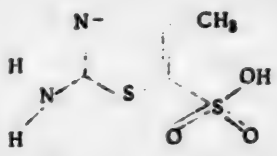
In the light of all the foregoing facts, we can confidently conclude that in the sulfamides of 2-acetamino-4-methylthiazole and correspondingly in the sulfamides of 2-acetaminothiazole, the sulfamide group is in the 5-position of the thiazole ring. It, therefore, follows that also in the starting sulfochloride of 2-acetamino-4-methylthiazole, the SO_2Cl group is in the same position, i.e., the sulfochloride is a derivative of the sulfonic acid (III) and has structure (XII).

At the start of the paper it was indicated that on hydrolysis the sulfochloride changes into the acid with m.p. 253° to which Ochiai and Nagasawa [1] and later Hurd and Kharasch [5] assigned the structure of the sulfamic acid (II). These conclusions were based mainly on the fact that the acid with m.p. 253° rearranges to the higher melting acid, which they assumed to be the sulfonic acid. In explanation of this phenomenon of rearrangement in the 2-aminothiazole series, an analogy was mechanically drawn with the known rearrangement of benzenesulfamic acid into sulfanilic acid.

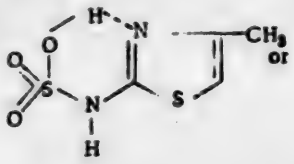
Since it has now been shown that the sulfochloride has structure (XII), it follows that the acid derived from it with m.p. 253° is the sulfonic acid (III); consequently, the acid into which compound (III) changes when heated with strong sulfuric acid must be regarded as the sulfamic acid (II).

This type of unusual rearrangement of a sulfonic acid into a sulfamic acid is here encountered for the first time. It is evidently associated, here in the 2-aminothiazole series, with the characteristic structure of the sulfamic acid (II).

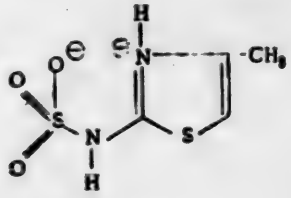
For this acid we can postulate a structure with an intramolecular hydrogen bond* (XIII) which strengthens the molecule; if this is correct, the possibility of transition from sulfonic acid (III) into sulfamic acid (XIII) becomes understandable:



(III)



(XIII)



(XIIIa)

The conclusions drawn in this paper about the structure of the sulfochloride and the products derived from it have been confirmed by the infrared spectra of the compounds here described.

EXPERIMENTAL

(With participation of V. V. Kushkina)

Preparation of Low-Melting Sulfonic Acid (III)

According to Hurd and Kharasch [5] the low-melting acid with m.p. 256° (with decomposition) is obtained by adding chlorosulfonic acid to 2-amino-4-methylthiazole in carbon tetrachloride solution. The yield of recrystallized acid by this method is about 40%. A better yield and an immediately pure acid can be obtained if the solution of amine in carbon tetrachloride is added to the chlorosulfonic acid.

17.5 g (0.15 mole) 2-amino-4-methylthiazole was dissolved in 75 ml freshly distilled carbon tetrachloride. The amine solution was added dropwise, with good stirring and cooling over a period of 3 hours, to 22 ml (0.3 mole) chlorosulfonic acid. Much hydrogen chloride was evolved during the reaction. The temperature was −12° at the start of the reaction and + 14° at the end. After addition of the whole of the amine, the mixture was poured on to ice. The white crystalline precipitate was filtered, washed with water and dried on a water bath. Yield 23 g sulfonic acid (79% of the theoretical). M.p. 253-256° (with decomposition).** After recrystallization from ten times the quantity of water, rectangular prisms were obtained; m.p. unchanged.

The same acid was prepared by Ochiai and Nagasawa [1] by the action of strong sulfuric acid with cooling on 2-amino-4-methylthiazole, and also by hydrolysis of the sulfochloride (XII) [2].

Preparation of High-Boiling Acid (II) (Sulfamic Acid)

To 30 ml strong sulfuric acid in a round-bottomed flask was gradually added, with cooling, 20 g freshly distilled 2-amino-4-methylthiazole. The solution was heated at 150-165° on an oil bath for 5 hours. The mixture was then cooled to 40-50° and run in a fine stream with stirring into iced water. The brown precipitate was drained, washed with water and dried in the air. Yield 26 g (76%). The acid was recrystallized from 650 ml water with addition of active carbon. The colorless, large, polyhedral prisms did not melt when heated to 350°.

Formation of the Acid Chloride from the Low-Melting Acid

9.4 g (0.1 mole) low-melting sulfonic acid (m.p. 254-256°) was added in the cold to a solution of 0.4 g (0.1 mole) NaOH in 15 ml water. The solution was evaporated to dryness in a beaker on a water bath. The salt was recrystallized from a little water.

To 7.7 g sodium salt (about 0.03 mole) in a round-bottomed flask, fitted with an air condenser, was added 17 ml acetic anhydride, and the mixture heated at the boil for 2 hours. The contents of the flask were then cooled, and the precipitate was filtered, thoroughly washed with ether and dried on a water bath (yield 8.8 g). The acetyl derivative of the sulfonic acid was stirred with 15 g PCl_5 (about 0.06 mole), the mixture was thoroughly triturated and

*Another possibility is the polar, betaine structure (XIIIa). The problem of the unusual structure of the sulfamic acid may be finally clarified by determination of the dipole moments of the sulfonic acids.

**Without correction.

then transferred to a small round-bottomed flask, fitted with a reflux condenser, and heated for 2-2½ hours on a water bath. The mixture was gradually diluted during this process. After the conclusion of the reaction and cooling of the reaction mixture, ice was added to it. The curdy yellow product was filtered off, washed with cold water and dried in the air. M.p. 134-136°. Two recrystallizations from trichloroethylene gave 1.2 g colorless needles with m.p. 156-157°. A mixed sample with the sulfochloride prepared by the action of chlorosulfonic acid on 2-acetamino-4-methylthiazole melted without depression.

The same sulfochloride with m.p. 156° was obtained by the action of chlorosulfonic acid on the sodium salt of the acetyl derivative. The yield, however, was low (8.8 g salt gave 0.9 g sulfochloride).

Determination of Active Hydrogen in 2-Acetamino-4-methylthiazole

The investigated sulfamides are poorly soluble in anisole and amyl ether, but readily soluble in pyridine; all the active hydrogen determinations were, therefore, performed in pyridine solution.

The following method was found convenient for the preparation of substantially perfectly dry pyridine. After drying the pyridine by the usual method (distillation over KOH), it was transferred to a distilling flask and methylmagnesium iodide in anisole was added until bubbles of methane ceased to come off; then a small additional amount of methylmagnesium iodide was added and the pyridine distilled into a receiver provided with means for excluding atmospheric moisture. The pyridine so prepared did not cause methane evolution in a blank test with organomagnesium compound.

0.1385 g sub.: 23.2 ml CH_4 (24°, 740 mm). 0.2658 g sub.: 50.8 ml CH_4 (24°, 741 mm). Found active hydrogen (Chugaev-Tserevitinov method): 1.07, 1.19. $C_6H_8ON_2S$. Active hydrogen calculated: 1.00.

2-Acetamino-4-methyl-5-thiazolesulfone-N-ethylanilide (VI)

2.5 g (0.01 mole) 2-acetamino-4-methyl-5-thiazolylsulfonyl chloride was gradually run at room temperature with stirring into a solution of 1.2 g (0.01 mole) ethylaniline in 5 ml dry pyridine. The mixture, after standing for 24 hours, was poured into 100 ml cold water. The light-yellow product was filtered, well washed with water and dried in the air. Yield 3 g (91%): m.p. 187-189°. Recrystallization from aqueous alcohol (1:1) gave 2.6 g colorless prisms; m.p. 188-189°.

2.900 mg sub.: 0.328 ml N_2 (22°, 726 mm). 4.090 mg sub.: 0.465 ml N_2 (23°, 726 mm). 0.1053 g sub.: 7.2 ml CH_4 (20°, 735 mm). 0.1081 g sub.: 7.6 ml CH_4 (24°, 741 mm). Found %: N 12.52, 12.54; active hydrogen content (Chugaev-Tserevitinov) 0.93, 0.95. $C_{14}H_{17}O_3N_3S_2$. Calculated %: N 12.39; active hydrogen content 1.00.

Methylation of Compound (VI)

1.7 g (0.005 mole) substance (VI) was methylated in 1 N NaOH solution with dimethyl sulfate (2.5 ml). The product which separated on standing was filtered, washed with water, dried in the air and recrystallized from 35 ml dilute alcohol (1:1). Yield 1.3 g (74%); m.p. 128-129°. No change in m.p. after a second recrystallization. When the solution is cooled rapidly, the product crystallizes in rhombic form; on slow cooling it forms needles. The product does not react with CH_3MgI, i.e., it does not contain active hydrogen.

4.610 mg sub.: 0.495 ml N_2 (20°, 726 mm). 5.390 mg sub.: 0.557 ml N_2 (19°, 726 mm). Found %: N 11.95, 11.63. $C_{15}H_{19}O_3N_3S_2$. Calculated: N 11.89.

2-Acetamino-4-methyl-5-thiazolesulfone-dimethylamide (IX)

5.6 g (0.02 mole) sulfochloride (XII) was dissolved in 10 ml dry pyridine. Through the solution, externally cooled with ice, was passed a steady stream of dimethylamine prepared by decomposition of dimethylamine hydrochloride with alkali and drying over KOH. After saturation with dimethylamine, the solution was diluted with 100 ml water and then acidified with acetic acid to separate the amide. Yield 4.9 g (93%). M.p. 242-243°. Recrystallization from dilute alcohol (1:1) gave colorless leaflets with the same melting point.

Analysis for nitrogen by Pregl's method gave results 1% too low. Correct results were obtained in Kjeldahl analyses (semimicro).

0.0410 g sub.: 4.76 ml 0.1 N H_2SO_4. 0.0394 g sub.: 4.53 ml 0.1 N H_2SO_4. 0.0385 g sub.: 4.43 ml 0.1 N H_2SO_4. 0.1403 g sub.: 13.2 ml CH_4 (17°, 729 mm). 0.1819 g sub.: 16.8 ml CH_4 (17°, 732 mm) Found %: N 16.25, 16.09, 16.10; active hydrogen content (Chugaev-Tserevitinov) 0.99, 0.98. $C_8H_{11}O_3N_3S_2$. Calculated %: N 15.96; active hydrogen 1.00.

SUMMARY

1. It is shown that the action of chlorosulfonic acid on 2-acetamino-4-methylthiazole gives 2-acetamino-4-methylthiazole-5-sulfochloride (XII). Hydrolysis of the sulfochloride gives a sulfonic acid with m.p. 253-256°. The structure of a sulfamic acid attributed to this acid by Ochiai, Hurd and other authors is erroneous.

2. The observed transformation, on heating with strong sulfuric acid, of the acid with m.p. 253-256° into an acid with decomposition temperature above 340° must be regarded as an unusual case of transformation of a sulfonic acid (III) into a sulfamic acid (II) possessing the characteristic structure (XIII) or (XIIIa).

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PREPARATION AND PROPERTIES

OF 1,3-DIHYDROXYETHYLTETRAHYDRO-1,3-DIAZINE AND 2-PHENYLOXAZOLIDINE

K. D. Petrov, E. S. Lagucheva and V. I. Pukhova

In a paper published in 1949, Paquin [1] states that ethanolamine reacts with formaldehyde to form 1,3,5-trihydroxyethylhexahydro-1,3,5-triazine. According to our own observations, however, this reaction proceeds with formation of 1,3-dihydroxyethyltetrahydro-1,3-diazine (II) (see [2]). In agreement with the experimental data the reaction of ethanolamine with formaldehyde may be represented by the following equation:

$$2HOCH_2CH_2NH_2 + 2CH_2O \rightleftharpoons 2[HOCH_2CH_2NHCH_2OH] \xrightleftharpoons{2H_2O} 2HOCH_2CH_2N=CH_2 \rightleftharpoons$$

$$\rightleftharpoons HOCH_2CH_2-N\begin{matrix}CH_2\\ \diagup\quad\diagdown\\ CH_2\end{matrix}N-CH_2CH_2OH \qquad (1)$$

(II)

Experiments show that this reaction is best performed in benzene, the water being eliminated from the sphere of reaction with the solvent. This facilitates the left-to-right course of reaction (1) and the formation of the dihydroxyethyldiazine in a purer form.

The dihydroxyethyldiazine has the appearance of a viscous, colorless oil, n_D^{20} 1.5132. On heating followed by distillation, it changes into a readily mobile liquid with n_D^{20} 1.4740. On standing, however, this liquid again quickly changes into the dihydroxyethyldiazine. It is interesting to note that the process of transformation of the liquid into the dihydroxyethyldiazine sometimes proceeds so energetically that the temperature rises to 70-90°. Concerning the structure of the liquid, this could not be established by a direct method, due to its instability. It is extremely probable, however, that it is methyleneethanolamine (I) whose formation from the dihydroxyethyldiazine (II) proceeds according to equation (2)

$$HOCH_2CH_2-N\begin{matrix}CH_2\\ \diagup\quad\diagdown\\ CH_2\end{matrix}N-CH_2CH_2OH \xrightleftharpoons[\text{spontaneous formation}]{\text{on heating}} 2HOCH_2CH_2-N=CH_2 \qquad (2)$$

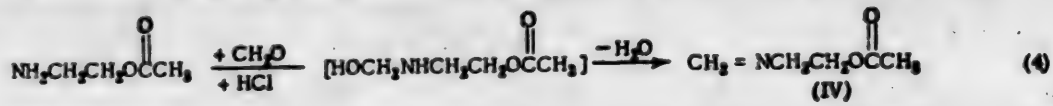
(II) (I)

This is clear from the following fact. On acetylating the dihydroxydiethyldiazine with acetic anhydride and attempting to distil the product of acetylation in vacuum, we obtained in place of the expected diacetyl derivative of the dihydroxyethyldiazine (III) the acetate of methyleneethanolamine (IV). The formation in this case of the acetate of methyleneethanolamine can be explained as follows. Acetic anhydride first acts on the dihydroxydiethyldiazine to form the diacetate of the dihydroxyethyldiazine (III). In the course of the distillation, however, (III) depolymerizes with formation of the acetate of methyleneethanolamine (IV) as represented by equation (3)

$$CH_3COCH_2CH_2-N\begin{matrix}CH_2\\ \diagup\quad\diagdown\\ CH_2\end{matrix}N-CH_2CH_2OCCH_3 \longrightarrow 2CH_2=NCH_2CH_2OCCH_3 \qquad (3)$$

(III) (IV)

Formation of methyleneethanolamine acetate (IV) was confirmed by analysis for nitrogen and molecular weight determination. Apart from this, we prepared for comparison the same acetate by another route (4)



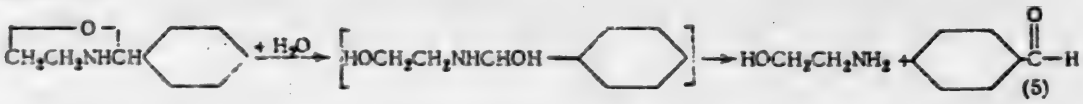
(4)

Methyleneethanolamine acetate prepared by route (4) corresponded in boiling point, specific gravity and refractive index to the product (IV) obtained in the process of distillation (heating) of the diacetate of the dihydroxyethyldiazine (III). It was thus proved that the product of depolymerization of the diacetate of the dihydroxyethyldiazine is undoubtedly methyleneethanolamine acetate. At the same time it was confirmed that the above scheme (2) for transition of the dihydroxyethyldiazine itself into methyleneethanolamine corresponds to the facts.*

Subsequently, we studied the reaction of the dihydroxyethyldiazine with β-hydroxypropylaniline, when it was observed that, when performing the reaction in non-anhydrous alcohol, ethanolamine and 5-methyl-3-phenyloxazolidine were formed. It goes without saying that the formation of these compounds is bound up with the conversion of the dihydroxyethyldiazine into ethanolamine and formaldehyde; we actually isolated the ethanolamine in the free state. The formaldehyde formed in these conditions reacts in known manner [3] with β-hydroxypropylaniline to form 5-methyl-3-phenyloxazolidine.

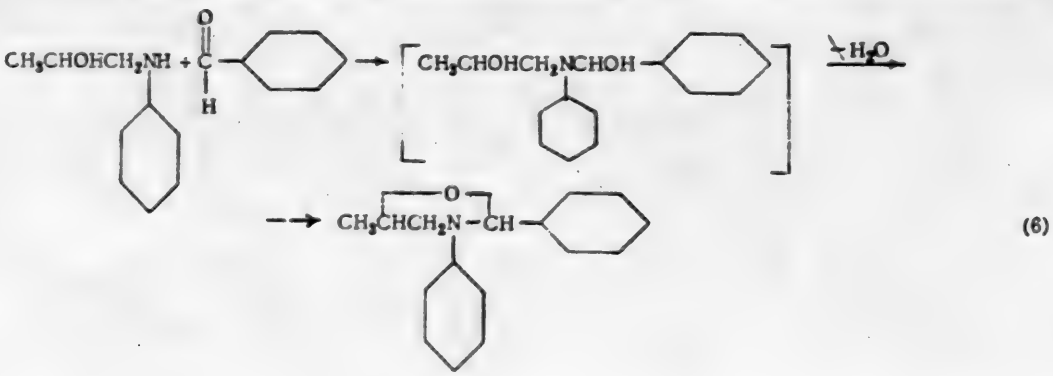
Concerning the mechanism of transformation of the dihydroxyethyldiazine into ethanolamine and formaldehyde, this is self-evident. The process is the reverse of the formation of the dihydroxyethyldiazine from ethanolamine and formaldehyde, as indicated by the right-to-left arrow in equation (1).

In this investigation we also studied the action of β-hydroxypropylaniline on 2-phenyloxazolidine. It was established that in alcoholic solution ethanolamine is also displaced from 2-phenyloxazolidine. The mechanism of the process proved to be similar to that of the preceding one, i.e., to the transformations of the dihydroxyethyldiazine which the latter undergoes when acted upon by β-hydroxypropylaniline, as shown by the following schemes (5, 6)



(5)

The benzaldehyde formed then reacts with β-hydroxypropylaniline to give 5-methyl-2,3-diphenyloxazolidine (V)



(6)

(V)

This observation is of interest since it illustrates some general properties of dihydroxyethyldiazine with oxazolidine derivatives: hydrolysis, formation of the same type of intermediate compounds (methylolethanolamines) and cleavage of the latter into aminoalcohols and aldehydes.

* Paquin considers that the 1,3,5-trihydroxyethylhexahydro-1,3,5-triazine described by him depolymerizes on heating with formation of the oxazolidine. The author did not, however, establish the formation of the oxazolidine, nor, strictly speaking, did he demonstrate the formation of the 1,3,5-trihydroxyethylhexahydro-1,3,5-triazine itself.

EXPERIMENTAL*

1. Preparation of 1,3-Dihydroxyethyltetrahydro-1,3-diazine (II)

Into a three-necked flask, fitted with stirrer, reflux condenser and water trap, were charged 122 g (2 moles) ethanolamine and 140 ml benzene. From a dropping funnel was gradually run in, with stirring, 163 g (36.70%) formaldehyde (approximately 2 moles CH_2O). At first the reaction proceeded spontaneously with evolution of heat; later the reaction mixture was heated on a bath to the boil. Water was removed from the sphere of reaction with the benzene vapor and collected in the trap. The process was continued until water ceased to come off. At the conclusion of the process, the reaction mass was fractionated in vacuum. Benzene and other volatiles (traces) were taken off in a low vacuum. An intermediate fraction came over at 60-92° and 6 mm in the form of a readily mobile colorless liquid, 22 g. On standing, this liquid changed into a viscous oil whose refractive index (n_D^{20} 1.51...) was close to that of the dihydroxyethyldiazine. The main fraction came over at 92-97° and 6-6 mm and was a readily mobile, colorless liquid — methyleneethanolamine (I). Yield 88 g (60.28%). It was redistilled for further purification to give a narrower cut with boiling range 94-97° at 6 mm, 48 g; n_D^{20} 1.4740. After brief standing this liquid changed (with heat development) into a viscous, colorless oil whose nitrogen content and molecular weight corresponded to 1,3-dihydroxyethyltetrahydro-1,3-diazine (II); numerous observations show that the change of methyleneethanolamine into the dihydroxyethyldiazine is substantially completed after 6-10 hours. In the air the dihydroxyethyldiazine absorbs an appreciable amount of carbon dioxide.

d_{20}^{20} 1.1787; n_D^{20} 1.5192; MR_D 38.30; Calc. 38.63.

1.1233 g substance: 151.32 ml 0.1 N H_2SO_4. 1.3158 g substance: 176.66 ml 0.1 N H_2SO_4. 0.3200 g substance: 34.98 g water: Δt 0.115°. 0.3407 g substance: 35.14 g water: Δt 0.12°. Found %: N 18.85, 18.79; M 147.14, 149.47. $C_6H_{14}O_2N_2$. Calculated %: N 19.13; M 146.

We also performed the reaction of ethanolamine with formaldehyde in the conditions described by Paquin [1], i.e., without removing the water from the sphere of reaction. The dihydroxyethyldiazine was then obtained in an insufficiently pure form and we were unable to purify it by repeated fractionations. The dihydroxyethyldiazine obtained by this method had the following constants:

d_{20}^{20} 1.1846; n_D^{20} 1.5136.

0.4259 g substance: 0.7938 g CO_2; 0.3805 g H_2O. 1.1635 g substance: 146.60 ml 0.1 N H_2SO_4. 1.5564 g substance: 194.60 ml 0.1 N H_2SO_4. 0.2250 g substance: 32.32 g water: Δt 0.09°. 0.2409 g substance: 37.17 g water: Δt 0.085°. Found %: C 50.83; H 9.99; N 17.54, 17.49; M 143, 141. $C_6H_{14}O_2N_2$. Calculated %: C 49.39; H 9.59; N 19.13; M 146.

2. Acetylation of 1,3-Dihydroxyethyltetrahydro-1,3-diazine

To 219 g (1.5 moles) 1,3-dihydroxyethyltetrahydro-1,3-diazine was gradually added from a dropping funnel 459 g (4.5 moles) acetic anhydride. After the whole amount had been added, the reaction mixture was heated for 8 hours at 95-100°. At the conclusion of the reaction, the excess anhydride was distilled off on an oil bath under vacuum; the mixture was then heated with 85 ml water and neutralized with saturated sodium carbonate solution. The product was repeatedly extracted from the aqueous solution with butanol and ether in the ratio of 1:1 by volume. The extracts were collected together and distilled. The solvent came over first; the ether was taken off at normal pressure and the butanol under low vacuum. Fractionation of the residue gave a main fraction at 107-109° and 7 mm weighing 115 g. This product was a readily mobile, colorless liquid. In nitrogen content and molecular weight it corresponded to the acetate of methyleneethanolamine (IV); b.p. 224-225° at 758 mm.

d_{20}^{20} 1.1474; n_D^{20} 1.4758; MR_D 28.30; Calc. 28.64 (without allowance for the double bond of $CH_2 = N$, whose value is not given in the literature). 0.3710 g sub.: 31.16 ml 0.1 N H_2SO_4. 1.0173 g sub.: 82.97 ml 0.1 N H_2SO_4. 0.9325 g sub.: 36.98 g water: Δt 0.405°. 1.5793 g sub.: 36.98 g water: Δt 0.71°. Found %: N 11.75, 11.42; M 115, 111.5. $C_5H_9O_2N$. Calculated %: N 12.17; M 115.

3. Preparation of Acetate of Methyleneethanolamine (IV) from β-Acetoxyethylamine and Paraformaldehyde

Into a flask, fitted with stirrer, reflux condenser and trap, were charged 51.5 g (0.5 mole) β-acetoxyethylamine, prepared by the method of Crane and Rydon [4], 16.5 g paraformaldehyde (0.55 mole CH_2O), 100 ml

*The molecular weights given in this paper were determined by A. L. Cherborovskaya, to whom we express our thanks.

benzene and 5 ml hydrochloric acid(sp. gr1.19). The reaction was performed with heating and continuous stirring. The water formed during the reaction was entrained by the benzene and collected in the trap. The process was continued until water ceased to come off (10 ml was collected in all). At the end of the process, the product was neutralized with sodium carbonate solution, extracted with butanol and fractionated in vacuum. The methylene-ethanolamine acetate fraction was collected at 100-105° and 7-6 mm in amount of 30 g. For further purification it was redistilled to give a product with b.p. 103-104° at 6 mm, 14 g. Readily mobile liquid with b.p. 224-226° at 761 mm.

d_{20}^{20} 1.1485; n_D^{20} 1.4762; MR_D 28.29; Calc. 28.64.

0.6001 g substance: 68.95 ml 0.1 N H_2SO_4. 0.7368 g substance: 82.80 ml 0.1 N H_2SO_4. 0.8606 g substance: 34.88 g water: Δt 0.42°. Found %: N 12.06, 11.94; M 108.67. $C_5H_9O_2N$. Calculated %: N 12.17; M 115.

4. Interaction of 1,3-Dihydroxyethyltetrahydro-1,3-diazine with β-Hydroxypropylaniline

In a flask with a ground-glass stopper were placed 72.8 g (0.498 mole) 1,3-dihydroxyethyltetrahydro-1,3-diazine, 120.8 g (0.8 mole) β-hydroxypropylaniline with b.p. 132-133° at 3 mm (n_D^{20} 1.5620) and 50 ml ethyl alcohol (not anhydrous). The reaction was conducted at room temperature for 8 hours. From time to time the mixture was shaken. The alcohol was distilled off on the boiling water bath when the reaction was concluded. The residue was distilled in vacuum through the column described by Kazansky and co-workers, fitted with a Whitmore-Luker condenser and Fenske packing. The following fractions were collected:

1 60-82° at 8 mm – 9 g, n_D^{19} 1.4558;
2 82-85° at 8-10 mm – 23 g, n_D^{19} 1.4561;
3 85-130° at 10-11 mm – 7 g, n_D^{20} 1.5559;
4 130-132° at 10-11 mm – 21 g, n_D^{20} 1.5600;
5 122-134° at 10- 9 mm – 10 g, n_D^{20} 1.5600;
6 124-146° at 9-11 mm – 20 g, n_D^{20} 1.5605;
7 146-158° at 11-10 mm – 25 g, n_D^{20} 1.5625.

Of these fractions, the 2nd, 4th, and 5th were examined more closely. The second fraction was distilled at 762 mm to give 8 g substance with b.p. 170-173°. In boiling point and refractive index (n_D^{20} 1.4560) it corresponded to ethanolamine, the literature values for which [6] are b.p. 171° and n_D^{20} 1.4539. The product collected at 130-132° and 10-11 mm (4th fraction) solidified on standing to a white crystalline mass, readily soluble in alcohol. After two recrystallizations from alcohol, it melted at 37.5-38.5°. In melting point it was identical with 5-methyl-3-phenyloxazolidine (m.p. 37-38°) as described by Kon and Roberts [3]. A mixed sample with the 5-methyl-3-phenyloxazolidine prepared by the method of Kon and Roberts melted at 37.5-38.5°. The analytical data also corresponded to 5-methyl-3-phenyloxazolidine.

0.1485 g substance: 0.3993 g CO_2; 0.1131 g H_2O. Found %: C 73.34; H 8.50. $C_{10}H_{13}ON$. Calculated %: C 73.60; H 7.97.

The fifth fraction also solidified on standing to a white crystalline mass and was 5-methyl-3-phenyloxazolidine, melting after two recrystallizations from alcohol at 37.5-38.5°.

5. Interaction of 2-Phenyloxazolidine with β-Hydroxypropylaniline

37.25 g (0.25 mole) 2-phenyloxazolidine, prepared by the method of Knorr and Matthes [7] (b.p. 132-134° at 9-7 mm, n_D^{19} 1.5700), was stirred with 37.72 g (0.25 mole) β-hydroxypropylaniline and 50 ml alcohol (not anhydrous). The mixture was mechanically stirred for 8 hours at room temperature; the alcohol was then driven off on a boiling water bath and the residue fractionated in vacuum, the following being collected: 1st fraction, 35-141° at 30-9 mm, 30 g; 2nd fraction, 141-180° at 9-8 mm, 26 g; 3rd fraction, 180-193° at 8 mm, 16 g.

Of these the 1st and 3rd were examined; the 1st fraction was distilled at atmospheric pressure to give 2 g substance with b.p. 169-172° (n_D^{20} 1.4500), identified as ethanolamine [7]. The 3rd fraction solidified on standing to a white crystalline mass. The crystals were washed with alcohol. Yield 9 g. The product was subsequently washed with sodium carbonate solution and recrystallized from alcohol; it then melted at 87.2-88.5°. Its melting point was identical with that of 5-methyl-2,3-diphenyloxazolidine (m.p. 88.5-89.5°) and a mixture did not give a depression (the mixture melted at 87.2-88.5°). The analytical data also corresponded to 5-methyl-2,3-diphenyloxazolidine (V).

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0.1410 g substance: 0.4242 g CO_2; 0.1014 g H_2O. 0.6958 g substance: 26.98 ml 0.1 N H_2SO_4. Found [illegible] %: C 80.12; H 7.85; N 5.43. $C_{10}H_{13}ON$. Calculated %: C 80.33; H 7.12; N 5.65.

SUMMARY

1. The preparation of 1,3-dihydroxyethyltetrahydro-1,3-diazine and of the product of its acetylation is [illegible] is described.

2. It was established that the product of acetylation of 1,3-dihydroxyethyltetrahydro-1,3-diazine polym[illegible] polymerizes when heated in vacuum and forms methylene-β-acetoxyethylamine.

3. It is shown that 1,3-dihydroxyethyltetrahydro-1,3-diazine reacts with β-hydroxypropylaniline to form [illegible] form ethanolamine and 5-methyl-3-phenyloxazolidine. A mechanism of this reaction is given.

4. The reaction of displacement of ethanolamine from 2-phenyloxazolidine by aromatic aminoalcohols [illegible] alcohols is described. This phenomenon of hydraminolysis is here described for the first time.

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Institute of Research on Plastic Materials [illegible] rials

SYNTHESIS OF DERIVATIVES OF 1-HYDROXYPHENAZINE

V. HALOGEN DERIVATIVES OF 1-METHOXYPHENAZINE

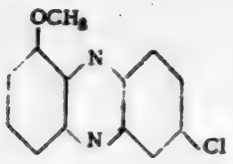
S. B. Serebryany and N. A. Ilyushina

In the first communication the synthesis of monochlorophenazines and of some dichlorophenazines was described [1].

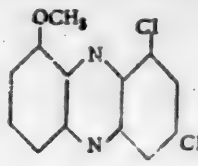
In the present paper we consider the preparation of chloro derivatives of 1-methoxyphenazine. We prepared these compounds with the aim of further transforming them into chloro derivatives of N-alkylphenazin-one-1.

Chloro derivatives of 1-methoxyphenazine were synthesized by alkaline condensation of o-nitroanisole with m- and p-chloroanilines. From the mixture of phenazine bases obtained by condensation of o-nitroanisole with p-chloroaniline was isolated 1-methoxy-7-chlorophenazine with m.p. 209-210°. This preparation was recently obtained by Vivian [2] by a complicated route from a derivative of 2-nitrodiphenylamine.

On condensation of o-nitroanisole with m-chloroaniline we should expect two chloro derivatives of 1-methoxyphenazine.



(I)



(II)

(III)

From the mixture of phenazine bases formed in this condensation, we actually isolated two chloro derivatives of 1-methoxyphenazine: light-yellow needles with m.p. 165-166° (I), and orange-yellow needles with m.p. 184-185° (II).

The position of the chlorine atoms in these preparations was established in the following manner: m-nitroanisole was brought into condensation with p-chloroaniline; two phenazine bases were formed: light-yellow needles with m.p. 165-168° and light-yellow needles with m.p. 150-151° (III). Both substances with m.p. 165-166° did not give a depression in a mixed test. Consequently, they are both identical with 1-methoxy-6-chlorophenazine (I). Hence, it follows that the preparation with m.p. 184-185° (II) is 1-methoxy-8-chlorophenazine, while the preparation with m.p. 150-151° (III) is 3-methoxy-6-chlorophenazine. The last substance was obtained by Vivian, m.p. 151-152° [2].

Employment of the chromatographic technique for resolution of the products of condensation enabled us to detect some secondary products of alkaline condensation in these reactions. Condensation of o-nitroanisole with chloro derivatives of aniline gives, apart from chloro derivatives of 1-methoxyphenazine, derivatives of phenazine not containing methoxyl groups.

Thus, on condensation of o-nitroanisole with p-chloroaniline, 2-chlorophenazine is formed in addition to 1-methoxy-7-chlorophenazine. From the mixture of phenazine bases obtained by condensation of o-nitroanisole with m-chloroaniline, 1- and 2-chlorophenazines were isolated in addition to the 6- and 8-chloro derivatives of 1-methoxyphenazine. We also detected dimethoxyphenazines in the mixture of condensation products: from the products of condensation of o-nitroanisole with p-chloroaniline was isolated 1,7-dimethoxyphenazine, while the products of reaction of o-nitroanisole with m-chloroaniline included 1,8-dimethoxyphenazine.

EXPERIMENTAL

Alkaline condensation was conducted in a three-necked reactor which was equipped with a mercury-sealed stirrer and a reflux condenser. The latter was connected to the reactor via a Dean and Stark trap. Into the reactor were charged the nitro compound and the amine (in 1:1 molar ratio); potassium hydroxide powder was dropped in and toluene was added. The reaction mixture was boiled for 7 hours. At the end of the reaction the contents were cooled and poured into 1 liter water. The toluene layer was diluted with three times the volume of solvent and separated from the alkali solution. The solvent and the unreacted starting materials were distilled off with steam. The residue after the distillation was dissolved in dichloroethane and worked up with 20% hydrochloric acid (3-4 times with 100-150 ml each time). The combined acid extracts were filtered and treated with aqueous ammonia. The separated mixture of phenazine bases was dissolved in benzene and chromatographed on alumina. The chromatogram was developed with benzene. The phenazine derivatives distributed over the various zones were separated mechanically. Each zone was eluted with a mixture of alcohol and benzene. The solvents were drawn off to leave a small volume and the phenazine base was separated by treatment with 20% hydrochloric acid followed by precipitation with aqueous ammonia. In some cases for complete resolution of the mixture, the chromatogramming was repeated several times.

1-Methoxy-7-chlorophenazine. A mixture of 15.3 g o-nitroanisole, 12.8 g p-chloroaniline, 28 g KOH and 150 ml toluene was heated 7 hours. In all, 2.11 g of impure mixture of phenazine bases was obtained. Three zones were observed when the chromatogram was developed: lower one, light-yellow; middle one, yellow; top one, yellow-brown.

From the bottom zone was isolated 0.8 brownish-yellow needles with m. p. 135-138°. Crystallization from alcohol gave light-yellow needles with m.p. 139-140°. The preparation dissolves in 15% hydrochloric acid with a yellow color. A mixed test with 2-chlorophenazine did not give a depression. This substance is therefore 2-chlorophenazine. Yield 3.7% of the theoretical. From the middle yellow zone was isolated 0.45 g yellow needles with m.p. 198-202°. The preparation dissolves in 15% hydrochloric acid with a red color and contains chlorine. It was purified by recrystallization from ligroine. Brownish prisms with m.p. 209-210°.

Found %: N 11.32, 11.50. $C_{19}H_9ON_2Cl$. Calculated %: N 11.45.

The analysis and chemical properties of this preparation identify it as 1-methoxy-7-chlorophenazine (Vivian reports m.p. 209-211° [2]). From the top brownish-yellow zone was isolated 0.5 g substance with m.p. 150°. No change in m.p. after crystallization. This substance does not contain chlorine and dissolves in 15% hydrochloric acid with a brownish-red color. For analysis it was purified by crystallization from dilute acetic acid. Yellow needles with m.p. 150°.

Found %: N 11.63, 11.68. $C_{14}H_{12}O_2N_2$. Calculated %: N 11.66.

The preparation melts at the same temperature as 1,7-dimethoxyphenazine [3] and does not give a depression in admixture with it. Yield 2.1% of the theoretical. Total yield of phenazine bases 7.6% of theoretical.

1-Methoxy-6-chloro- and 1-methoxy-8-chlorophenazines. A mixture of 15.3 g o-nitroanisole, 12.8 g m-chloroaniline and 25 g KOH in 150 ml toluene was boiled for 7 hours. 3.51 g of a mixture of phenazine bases was isolated. Chromatographic resolution of the benzene solution gave three zones: lower one, light-yellow; middle one, yellow, and top one, brown-yellow. A mixture of compounds was found to be adsorbed in each zone. The eluates of the bottom and middle zones, after removal of the alcohol, were therefore again chromatogrammed on alumina. The bottom zone then yielded two substances:

1) 0.23 g greenish-yellow needles with m.p. 115-117°; this compound was located in the lower part of the chromatogram. It contains halogen and dissolves in 15% hydrochloric acid with a yellow color. Crystallization from alcohol gave light-yellow needles with m.p. 20-22°. A mixed test with 1-chlorophenazine did not give a depression.

2) 0.8 g brownish-yellow needles with m.p. 135-138°; the preparation contains halogen and dissolves in 15% hydrochloric acid with a yellow color. Crystallizes from alcohol as light-yellow needles with m.p. 139-140°. A mixed test with 2-chlorophenazine did not give a depression. Yield of chlorophenazines, 4.9% of the theoretical. Chromatogramming of the eluate of the middle zone from the original chromatographic treatment gives the following picture: in visible light two zones are not observed, but in ultraviolet light two zones can be clearly distinguished – a lower yellow one and an upper greenish-yellow one.

The usual treatment of the lower zone gave 1-methoxy-8-chlorophenazine in the form of small orange-yellow needles with m.p. 184-185°. The preparation was purified for analysis by crystallization from ligroine.

Small orange-yellow needles with m.p. 184-185°.

Found %: N 11.20, 11.16; Cl 14.40, 14.49. $C_{13}H_9ON_2Cl$. Calculated %: N 11.45; Cl 14.49.

From the upper greenish-yellow zone was isolated a substance with m.p. 140-152°. This was evidently a mixture of two phenazine bases. Repeated chromatogramming of the benzene solution of this mixture on alumina led to isolation of a compound with m.p. 160-161° and a further quantity of 1-methoxy-8-chlorophenazine with m.p. 184-185°. The 1-methoxy-6-chlorophenazine with m.p. 160-161° was recrystallized from aqueous alcohol prior to analysis. Yellow needles, m.p. 165-166°.

Found %: N 11.30; Cl 14.31. $C_{13}H_9ON_2Cl$. Calculated %: N 11.45; Cl 14.49.

Both preparations dissolve in 15% hydrochloric acid with a red color. A total of 1.65 g 1-methoxy-8-chlorophenazine with m.p. 184-185° was obtained and 0.57 g 1-methoxy-6-chlorophenazine with m.p. 160-161°. The yield of these bases was 9.1% of the theoretical. From the eluate of the upper brownish-yellow zone of the original chromatogram, after concentration of the solvent to a small volume, crystallized brownish-yellow needles with m.p. 254-255°. This substance does not contain halogen and dissolves in 15% hydrochloric acid with a dark-red color. For purification it was crystallized from ligroine. Long, filiform, bright-yellow needles with m.p. 259-260°. A mixed test with 1,8-dimethoxyphenazine [4] did not give a depression. From the mother liquor was isolated a mixture of phenazine bases. Chromatographic resolution of this mixture yielded a further quantity of 1,8-dimethoxyphenazine and a mixture of methoxychlorophenazines. A total of 0.15 g 1,8-dimethoxyphenazine was obtained. The total yield of phenazine bases obtained by condensation of o-nitroanisole with m-chloroaniline is 14.1% of the theoretical.

1-Methoxy-6-chloro- and 3-methoxy-6-chlorophenazines. A mixture of 7.7 g m-nitroanisole, 6.4 g p-chloroaniline, 13 g KOH and 75 ml toluene was boiled for 7 hours. Chromatographic resolution on alumina of the mixture of phenazine bases from benzene solution gave two zones: lower one, light-yellow and upper one, yellow. From the lower one was isolated brownish-yellow needles with m.p. 150-151°. The preparation dissolves in 15% hydrochloric acid with a yellow color. For analysis the preparation was purified by crystallization from aqueous alcohol. Small, light-yellow needles, m.p. 150-151°.

Found %: N 11.13. $C_{13}H_9ON_2Cl$. Calculated %: N 11.45.

From the upper zone was isolated a preparation with m.p. 160-162°, soluble in 15% hydrochloric acid with a red color. After crystallization from aqueous alcohol it melted at 165-166°. The yield of phenazine bases in this condensation is relatively low and amounts to 1.2% of the theoretical.

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SUMMARY

1. 1-Methoxy-7-chlorophenazine is obtained by alkaline condensation of o-nitroanisole with p-chloroaniline.

2. Condensation of o-nitroanisole with m-chloroaniline and of m-nitroanisole with p-chloroaniline gives a mixture of chloro derivatives of 1-methoxyphenazine: in the first case a mixture of 1-methoxy-6-chloro- and 1-methoxy-8-chlorophenazines; in the second a mixture of 1-methoxy-6-chloro- and 3-methoxy-6-chlorophenazines. These mixtures were resolved by chromatogramming of their benzene solutions on alumina.

3. Condensation of o-nitroanisole with chloroanilines gives, apart from derivatives of 1-methoxyphenazine, derivatives of phenazine and dimethoxyphenazines.

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*See Consultants Bureau Translation, page 1691.

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